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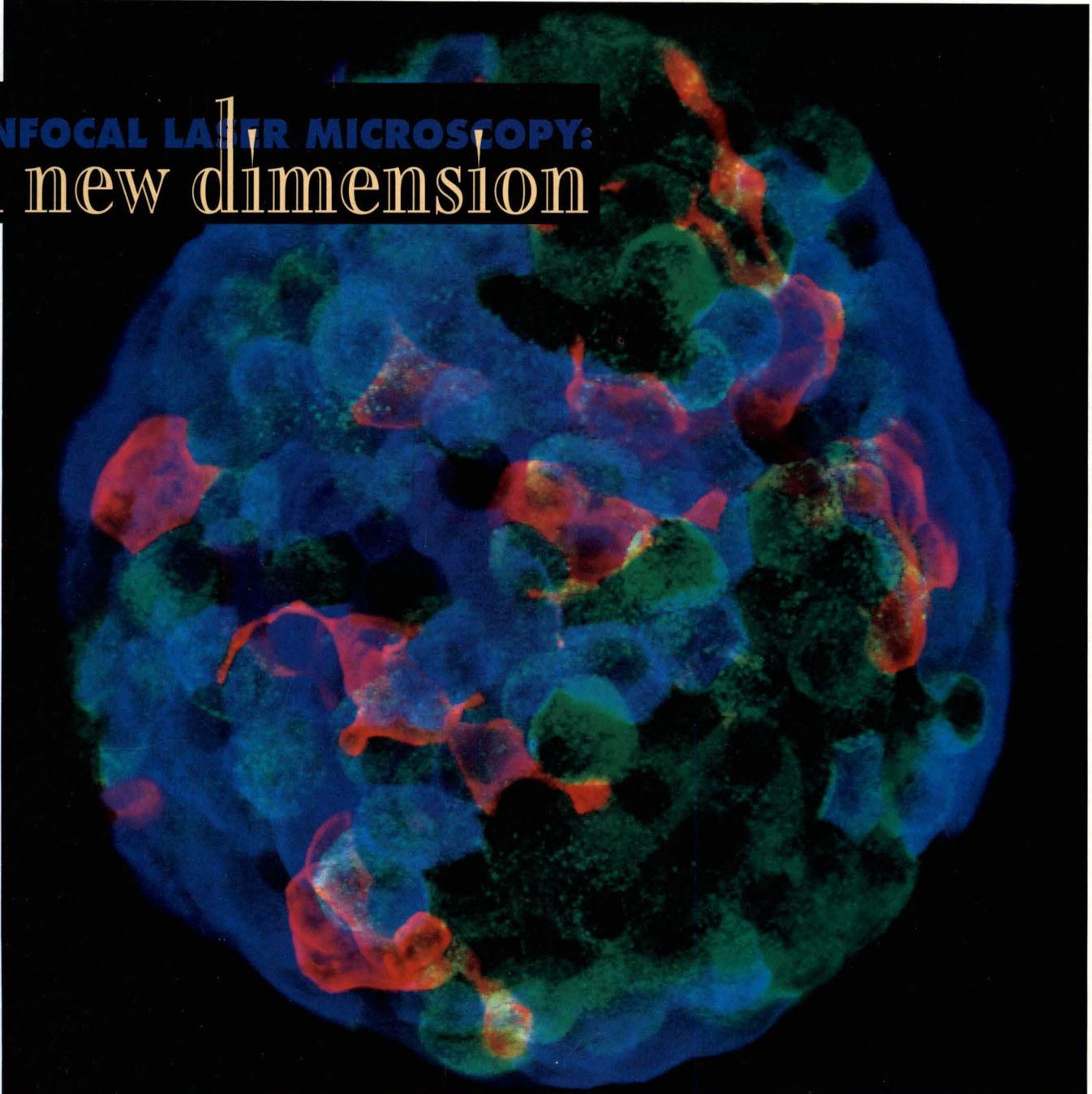
UNIVERSITY OF MINNESOTA

MEDICAL

BULLETIN

SUMMER 1992

ANFOCAL LASER MICROSCOPY:
A new dimension



A PUBLICATION OF THE MINNESOTA MEDICAL FOUNDATION

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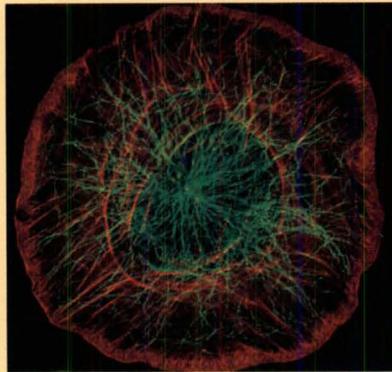
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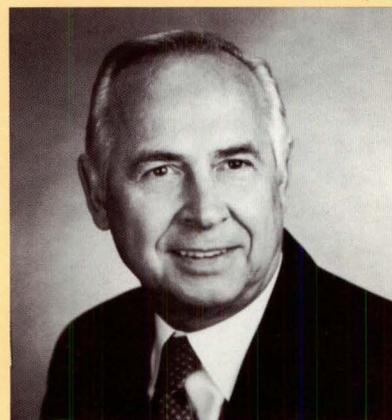
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On the Cover: New developments in confocal laser microscopy give a three-dimensional image of intact tissue. Pictured is a triple labeled rat islet of Langerhans demonstrating the presence of insulin containing B-cells (green), somatostatin containing D-cells (red), and glucagon containing A-cells (blue).

The Minnesota Medical Foundation supports the research and educational missions of the University of Minnesota Medical Schools by encouraging private contributions.



Depression: A Universal Disease

The human animal is characterized by a strong need for companionship and reinforcement. We long to share our pleasures, accomplishments, disappointments, anger, fears, and doubts with each other. Regardless of how we define stress, each of us has the need to express ourselves in a fashion which involves personal interaction and feedback. Self-doubt and an inability to interact with companions runs a great risk for a complete breakdown of self-esteem and the ability to cope.

The origin of depression, the self-realization of the depths of pain and despair, and the contemplation of life and other related matters are eloquently described in William Styron's autobiography *Darkness Visible — A Memoir of Madness*.

Mr. Styron is aware of recent debates about the genetics of depression, but attribution of even a component of depression to genetics does little to allay the fear accompanying that disorder. Undoubtedly, molecular geneticists working with psychiatrists will uncover both the specific gene location and eventually the precise biochemistry of some forms of "depression." Depression, now often treated as a singular disorder, will eventually be viewed as a mere symptom of a complex genetic and biochemical disorder. Will these discoveries lead to radical pharmacology to break the cycles for individuals with depression before they commit some form of self-destruction?

As Phillip Abelson described the probable complexity of several behavioral disorders as "nature vs. nurture," it would not be surprising that the environment will prove to have a significant role in their causes. What can we as health care professionals do to better understand ourselves and our patients? How can we better cope with the complex environments in which we exist?

As always, we should be alert, receptive, and responsive to the needs of others. We need to recognize our frailties. We should recognize common symptoms of problems—sometimes hidden

as diminished performance in the workplace, withdrawal from interaction with others, changes in behavior patterns, and chronic disturbance of normal sleep patterns. We would do well to recognize these changes in ourselves, our colleagues, co-workers, and certainly in our patients.

The calamity of suicide has become a dominant cause of death in adolescents (frequently associated with alcohol or drugs and often masked as accidents). Depression and suicide are particularly prominent in some minority groups where many familial and societal structures have crumbled or disappeared. Too many lives from all social and economic classes have been lost due to depression and suicide. The problem goes well beyond the highly publicized genius whose creativity has been linked with depressive behavior disorders. It has become a prevalent condition in our society, and it is a diagnosable and treatable disease that needs exposure, recognition, and acceptance.

As we attempt to contend with the trials and tribulations of health care delivery systems and the new economics, we must not forget that major psychiatric disorders such as depression deserve the same consideration as diseases that are accepted as "organic" in their origin. Depressed patients hurt, they lose productivity at work, they destroy the lives of those closest to them, and in many cases, these patients die. This is not a problem that only affects "someone else." The problem is universal. We all have friends or loved ones whose cries for help need answering. Each of us should be alert for the all too common warning signs of depression and despair. More importantly, we should make ourselves available to those in need and be prepared to intervene when they are not able to cope with all that life has to offer.

David M. Brown, M.D.

Dean

University of Minnesota Medical School

An added dimension

New developments in laser scanning confocal microscopy

Necessity was indeed the mother of invention when a group of researchers found that an expensive new laser microscope couldn't provide the images they needed.

by Michael P. Moore

When Anton van Leuwenhoek first looked in his microscope and saw little bodies (microbes), he started a drive for ever greater microscopic viewing and imaging technologies. The University of Minnesota Medical School's Department of Cell Biology and Neuroanatomy experienced a step in that drive in 1988 when a group of faculty took delivery of the latest in high-tech imaging systems: an argon laser scanning confocal microscope capable of produc-

ing three-dimensional photographs of biological specimens.

Little did they know that for the next three years a few of them would be consumed with efforts to harness and refine the scientific potential of the new instrument, and that when they were done, they would have helped to elevate the technology to a new plane of visualization and discovery.

Expectations were high when the confocal microscope arrived in 1988 from Bio-Rad, a world-wide marketer of scien-

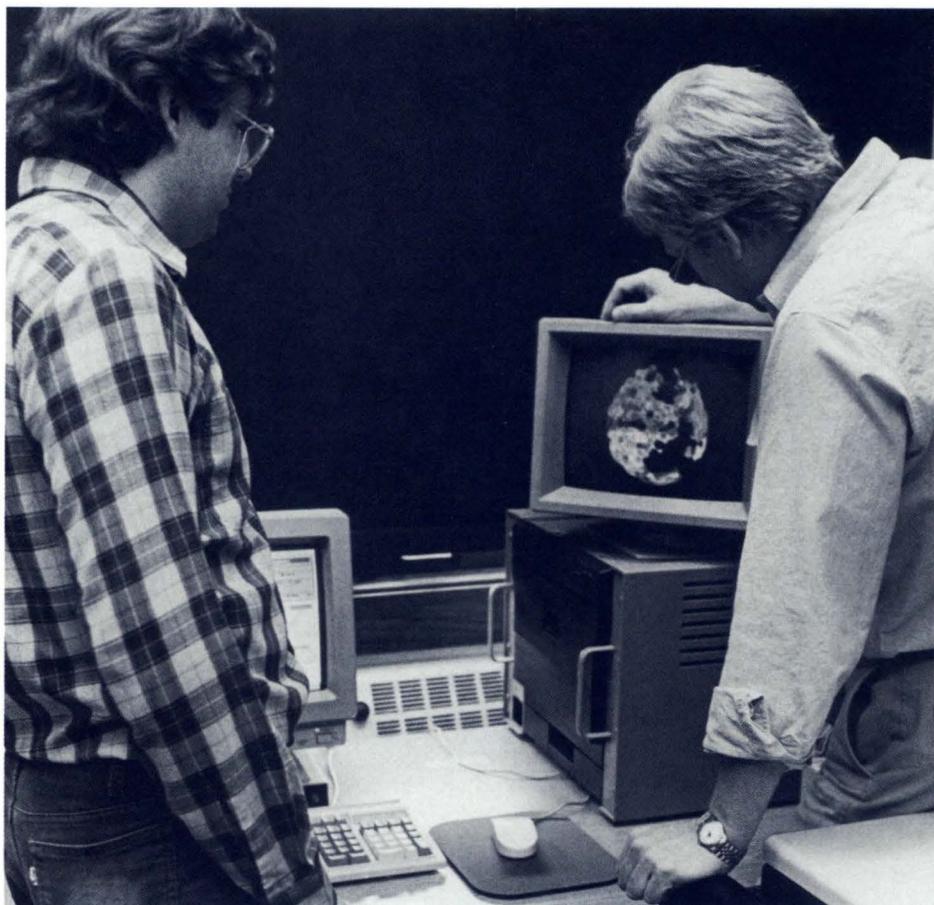
tific viewing and imaging systems. It was purchased for over \$130,000 with a shared instrumentation grant from the National Institutes of Health and partial funding from the Minnesota Medical Foundation. With multi-unit hardware as impressive as its price, the system was intimidating yet irresistible.

Professor Robert Sorenson, whose lab has been most closely involved with the confocal microscope, explains why it was so alluring:

"With a conventional light microscope you need to section tissue with a microtome, which provides slices 5 to 10 microns thick. Then you stain the sections and view each individually. This gives you a two-dimensional view of each thin slice. To get an idea what the structure looks like in three dimensions, you have to prepare and image many sections, store them in a computer, and reconstruct them sequentially. Even with the best technique you're going to have artifacts caused by the degradations where the knife cut each surface. And when you try to reconstruct the slices it's very hard to get good registration and focus.

"With a confocal microscope there is no need to cut thin sections. The laser scanning confocal technology allows one to optically section thick tissue specimens, up to about a 100-micron practical limit. You can relatively quickly step down through the tissue and information goes back to the computer, which reconstructs all the images and gives you a three-dimensional image of the still intact tissue.

"In our laboratory we look at islets of Langerhans [pancreatic structures that secrete various hormones, including insulin]. In a few minutes we can focus on things that are of interest. For example if you see a nerve coming into an area you can follow that nerve for some distance as it winds its way through the tissue. If you were trying to do this through sliced sections you'd very quickly lose the nerve. Because of the ease with which you can study structures in three dimensions, you can look at things that you never would have ventured to try if you



PHOTOS BY NANCY MELLGREN.

were using physical sections.

"I've been looking at islets for 20 years, and the first day we stained islets and looked at them with confocal microscopy, I was wide-eyed. Wow!"

Improving the system

One of the first to grapple with the technicalities of using the confocal microscope was Todd Brelje, a graduate student in Sorenson's laboratory. He was able to figure out how to print relatively clear and impressive 3-D images with the system, but it was soon clear that it had major limitations as a research tool.

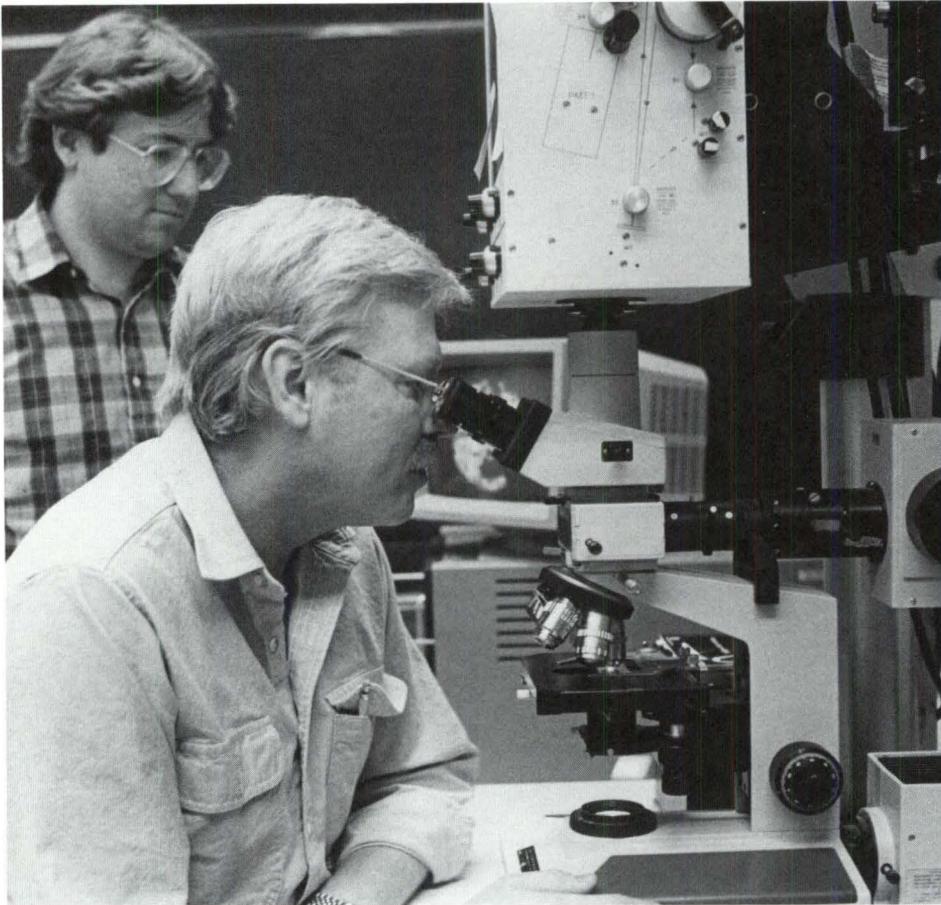
"You could make it do what the company said it could do, but only under very defined conditions," Brelje recalls. "It wasn't a very good research tool, because prior to looking at something you had to decide what you wanted to see and what it was going to look like. You could get some two-color images by adjusting how well you stained your tissue. But it only worked because you knew what you were supposed to get. You could use two dyes, but you'd get quite a bit of bleed-through in your

Graduate student Todd Brelje (left) and Cell Biology & Neuroanatomy Professor Robert Sorenson produce 3-D images with the laser scanning confocal microscope.

sample, so you really couldn't tell if the things you were looking for were in the same cell, or if the stain had just bled through."

Rather than giving up on the instrument's great potential, Sorenson and Brelje set out to find a way to make it work better for their research needs. Brelje hit the books, boning up on the latest literature on laser imaging. He found that the field of flow cytometry, which basically involves counting specific types of cells, was ten years ahead of the imaging field in its use of lasers to excite dyes at different wave lengths to get different colors. He reasoned that by using more than one laser it might be possible to get different colors of light output that would more clearly define the images viewed with the confocal microscope.

"The problem with the argon laser is that you can excite two things and they each have their own response, but if you're getting both responses simultane-



Brelje and Sorenson plan to use confocal laser microscopy to study the adaptation of pancreatic islets during pregnancy.

ously you have to try to filter out which one is coming from what," Brelje says. "It's like two people talking at the same time: it's hard to follow both of them, but you can get the gist of it. We needed a way to get different light output that could be filtered to sort out the different responses from two or three different dyes, and end up with a clear image."

Brelje found out that the Becton Dickinson company had accomplished this in the early 1980s, but with a room-sized system of four \$30,000 water-cooled lasers that would be impractical for routine scientific use. "So I started calling laser manufacturers to see if I could find someone who thought they could build a smaller air-cooled laser that would have different colors of useful light output."

He located a company, Interactive Laser Technology (ILT), that had built such a laser but had been able to sell only a few to the Food and Drug Administration for use in fruit inspection programs. ILT's engineers thought they could modify the laser to do what Brelje and

Sorenson were describing, but the company wanted to be paid ahead of time for the parts needed to develop it.

"The project might have died right there, because we couldn't pay a company to develop a tool that might not even do the job when it was finished," Sorenson says. But convinced that there would be a market for a confocal microscope equipped with the souped up laser, Brelje became a salesman for the idea.

"I contacted Bio-Rad to see if they would pay ILT to develop it. I convinced both companies that there would be a market for this kind of laser if they would get together and build one for us to test. We told Bio-Rad that we would order one from them if they would pay ILT to build it. We specified what we needed, and this resulted in a krypton/argon mixed gas laser, which took ILT a year to build. There were a lot of phone calls back and forth among the three parties to the deal, with each making sure the other was living up to its end of the agreement. In the end, ILT delivered the laser to Bio-Rad, which put it together with the filters they had developed for it according to our specifica-

The new imaging technology allows scientists to study things they couldn't in the past, and to study them far more efficiently.

tions, and sold it to us."

"We fired it up in the fall of 1990, and it worked; it did everything it was supposed to do," Sorenson says. "The project relied on everyone believing us that this thing would actually work. We could figure out which types of fluorescent dyes we needed to examine two and three structures in tissues, and then we had to determine the type of laser that would give us the color and light intensity needed, and then we designed the filters to separate the signals. We had the expertise in dyes and fluorescent microscopy, so when we were presented with the problem it was a matter of looking for possible solutions and talking to people who knew the laser engineering.

"The good thing is that Todd is very bright and has a broad knowledge of biology and technology, so he could translate what we needed biologically into language that the engineers could understand. So he was able to tell them exactly what we had to have and why we had to have it. I think that without Todd's capabilities and persistent involvement the project would have died, because we would have been faced with engineers who thought it was too difficult and didn't understand why it needed to be that way.

"When they became confident that they were talking to someone who really understood the nature of the problem, that's when they began to put their best efforts into responding. This wasn't an easy project for them, either. They initially thought it would be easy, but when they found out we wouldn't accept 'good enough,' it took a lot of additional effort to get it right. And I think the upshot is that everybody's really happy with the result."

Brelje didn't stop after directing the hardware revisions. He also felt it would be possible to improve the system's software to make it easier and more efficient for use in research. He became a consultant to Bio-Rad and during his spare time at home wrote the software the company now provides with its confocal systems.

Inventors for the 21st century

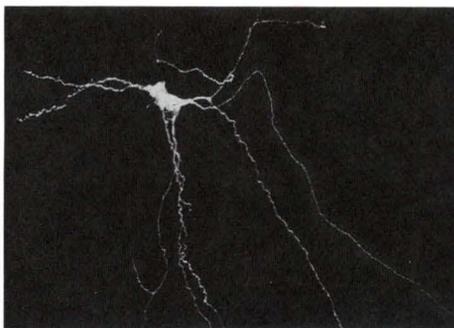
Because Brelje and Sorenson had conceived and directed the work on the krypton/argon laser confocal microscope, they were its inventors. And because that work was done using the University's resources, the invention belonged to the University of Minnesota. In October 1990 the University's Office of Patents and Licensing, working collaboratively with Bio-Rad attorneys, filed applications for U.S. and foreign patents on the invention. A license agreement was negotiated under which exclusive rights were granted to Bio-Rad to use the new laser for confocal microscopes, in return for royalties (a percentage of its sales) payable to the University.

As called for in the Regents Policy on Patents and Technology Transfer, the royalty payments will be split according to the following formula: 33% to the researchers, 25% to their laboratory research, 8% to their college (the Medical School), and 33% to the University for technology transfer activities. Royalty terms were negotiated at one level for sales occurring while the patent application is under review, and at a higher level when the U.S. patent is issued. The Office of Patents and Licensing was notified in January 1992 that the U.S. Patent and Trademark Office has allowed the patent and will issue it soon.

Representatives of Bio-Rad report that the krypton/argon laser has become its most popular light source for confocal microscopy, and that over 100 have been ordered already. Last November Brelje et al presented poster sessions including some of the first images generated with the new instrument at a neuroscience conference in New Orleans. "I was swamped with inquiries," he reports happily.

Although the krypton/argon confocal microscope is located in Sorenson's laboratory, it is used routinely by three other laboratory groups in Cell Biology and Neuroanatomy and by researchers from two laboratories in the College of Biological Science. Often, scientists from other departments use it "in cases where they aren't able to see something very well with their own conventional microscopes, and just being able to look at it with the confocal helps clarify things enough so that they can go back to their own laboratories and, knowing the structure of what they're studying, proceed

"I've been looking at islets for 20 years, and the first day we stained islets and looked at them with confocal microscopy, I was wide-eyed. Wow!"



Optical sectioning by confocal laser scanning microscopy aids in demonstrating an intact nerve cell and its extensive processes throughout a 300 um thick tissue specimen. This cell found in the locus coeruleus of the brainstem typically contains the neurotransmitter norepinephrine and was labeled with a fluorescent dye for imaging purposes. Image courtesy of M.W. Wessendorf and J.T. Williams.

with the research," Sorenson says.

He explains that the krypton/argon laser allows researchers to excite each one of three dyes individually, so they can examine either one, two, or all three distinct substances or structures that have been stained. "We now know that the signal we get is from a specific dye and only from that dye. With three colors we can stain three different cells or cell structures and put them all back together and look at them relative to each other to see how they relate, so it really opens up a lot more questions one can investigate.

"A recent example from our laboratory is when we were looking at the innervation of the islet. We had looked at GABA immunoreactivity in islets a few years ago and at that time we never appreciated the fact that there were nerves in the islet that contain GABA [a neurotransmitter that carries signals to cells]. When we went back to reexamine the issue of where GABA is located in the islets, that's when we discovered that there appear to be GABA nerves in the pancreas. These are very small cells and processes, which with conventional microscopy we never would have been able to convince ourselves that we were

actually looking at a nerve. With confocal laser microscopy we now can actually see those nerve cell processes penetrate into a portion of the islet."

Sorenson and colleagues also have been able to expand their studies of the relationship of the various hormones released by the pancreatic islets. "In the islets it is known that there is a heterogeneity among islet cells. Some beta [insulin-releasing] cells have more insulin in them than others, for example. If you study this with thin tissue sections, it's basically anecdotal. You look at them and say this cell looks like it has more insulin than the other one.

"Now that we can sample the entire islet we can easily look at substances other than insulin. We've found that in certain cases there's a correlation between the amount of one substance and that of another, and in other cases there's a negative correlation. We don't know the significance of these correlations yet, but the question wouldn't have even been there without the ability to scrutinize large samples of cells in the intact islets."

Given these new exploratory capabilities, Sorenson plans to examine questions related to the main focus of his laboratory: the adaptation of pancreatic islets during pregnancy. He hopes that the improved ability to study cell division and the kinds and amounts of hormones that regulate growth will shed light on both normal gestation and such abnormalities as gestational diabetes.

What it boils down to, Sorenson says, is that the new imaging technology allows scientists to study things they couldn't in the past, and to study them far more efficiently. He thinks that it will also have a major impact on science teaching and communication of biological knowledge.

"Having 3D images is so much more effective in communicating structural biology to students, to laypeople and to other scientists. You don't have to extrapolate from a stained slide of a thin slice of tissue what the cell or neuron actually looks like. And when you can see all the connections and structures in their natural state, that helps you ask good questions about function. It makes things more accessible."

Michael P. Moore is communications coordinator for the University of Minnesota's Office of Research and Technology Transfer Administration.

Getting tough

The University of Minnesota is part of a nationwide bone marrow transplant trial aimed at attacking breast cancer and other cancers.

by Peggy Rinard

"It was all worth it. In about February, my energy came back with a whoosh. And by spring I could do it all—play with the kids, ride my bicycle, garden, and mow the lawn."

Stephanie Daniels missed seeing her two young children off to school last fall. She was in the bone marrow transplant unit at the University of Minnesota Hospital and Clinic (UMHC) fighting back against her breast cancer, and hoping the experience would allow her to see them through many school years to come.

Daniels, 33, came to UMHc in the summer of 1991, after the breast cancer she had been treated for a couple of years back reappeared as tumors in her neck. She had exhausted her treatment options in St. Cloud, where she lives, and was sent to the Twin Cities for experimental alternatives. As it happened, James Radford, assistant professor of medicine, had just been named institutional investigator for the University's participation in a new national trial of bone marrow transplantation sponsored by the National Cancer Institute and Blue Cross/Blue Shield. He was looking for three women with advanced breast cancer for the first phase of the study.

"I visited other hospitals in the Twin Cities to find out what all of my options were. I chose the University because their treatment was the most aggressive," Daniels says. "I had confidence that I was doing the most I could to get rid of the cancer."

Daniels became the first University of Minnesota patient to go through the trial, which is breaking ground in several ways: It's the first multi-center, randomized trial of bone marrow transplantation for a solid tumor; it is testing new bone marrow transplantation methods that shorten hospitalization time and hopefully will enhance results; and it represents the first time a private, third-party payor has participated in a major clinical trial.

In the 20 years since the National Cancer Act kicked off the government's war on cancer, \$1 billion has been spent on breast cancer research. Advances in basic research have greatly increased understanding of the disease, but the payoff at the clinical level has been modest. The five-year survival rate in 1970 was 68 percent for caucasian women, 51 percent for blacks; from 1981-1986 it was 78 percent for caucasians, 64 percent for blacks.

Once cancer spreads it usually becomes a fatal illness. Chemotherapy, radiation therapy, and immunotherapy can slow but not stop the proliferation of malignant cells. The one hope that has emerged is that breast cancer is more responsive to chemotherapy than most other cancers. That is why it is one of the first solid tumors for which bone marrow transplantation is being extensively tested. Bone marrow transplantation allows higher doses of chemotherapy to be given while avoiding bone marrow failure, a frequent side effect of high-dose chemotherapy.

Improving the odds

The new trial is an all-out effort to get tough with breast cancer in response to the discouraging statistics in a group of women with a particularly poor prognosis. It was developed by the Cancer and Leukemia Group B (CALGB), a consortium of cancer researchers in the eastern United States, based on a pilot study at Duke University.

"Eighty percent of the women who participated in the pilot study are still free of their cancer at follow-ups as long as five years. For this particular group of women that's astonishing," Radford says.

Daniels, who had stage IV breast can-

with cancer

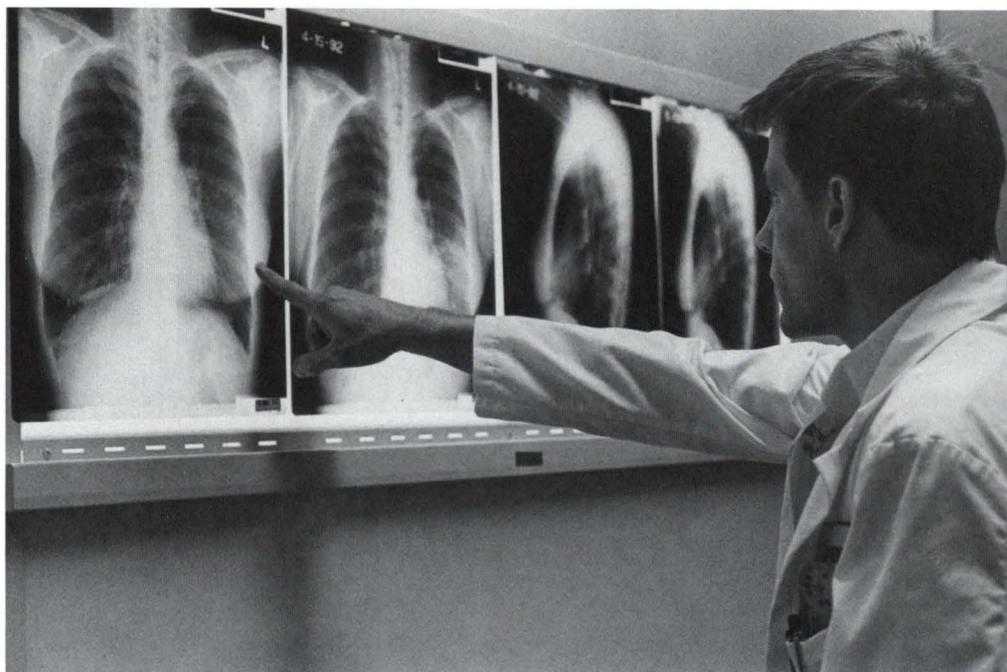
cer (tumor has spread beyond the breast and lymph nodes) when she came to UMHC, participated in the first phase of the study, which was a preliminary trial for women with advanced breast cancer. Most of the women enrolled will have stage II breast cancer (localized with lymph node involvement) which has spread to ten or more axillary nodes at the time of surgery. The trial is a lengthy one, and includes just about anything and everything that might work against breast cancer.

All women first receive four months of standard outpatient chemotherapy (cytoxan, adriamycin, and fluoruracil) after which they are randomized into two groups. Women in one group will have autologous bone marrow transplantation — their own marrow will be harvested and then reinfused after high dose chemotherapy and radiation.

Women in the other group will also get a round of high-dose chemo, but not enough to seriously damage bone marrow and they will not require bone marrow transplants. The high dose therapy for both groups is a combination of different agents than those used in the first round of chemo.

"Women in both groups will get more chemotherapy than is standard. We know that higher doses of chemotherapy are more effective against breast cancer. The specific question we're trying to answer here is whether bone marrow transplantation has a role, or if we can give enough chemotherapy without bone marrow transplantation," says Philip McGlave, professor of medicine, and director of the University's adult bone marrow transplantation program.

Both groups get a growth factor called G-CSF to boost white blood cell produc-

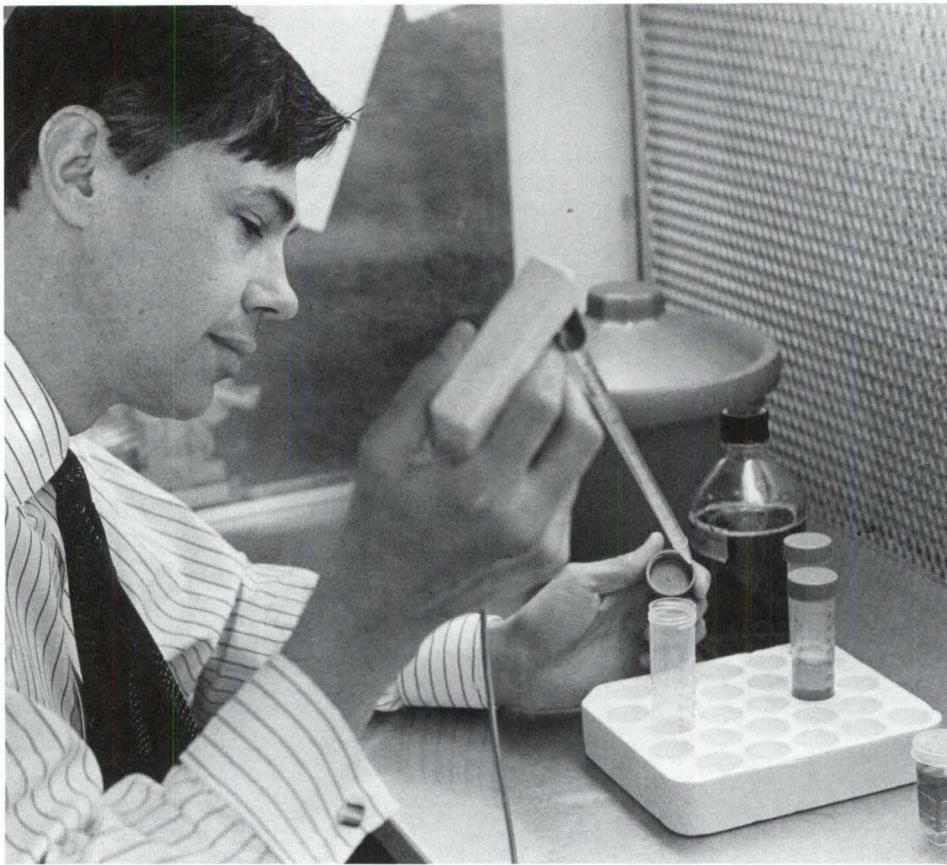


tion, followed by radiation, and, if their cancer is hormone-dependent, an anti-estrogen drug called Tamoxifen.

Patients in the transplant arm of the trial get a double-dose of stem cells, which give rise to new blood cells. They are given stem cells taken from their blood as well as bone marrow. It's a new twist in bone marrow transplantation.

"You can do a transplant with either peripheral stem cells or marrow cells alone. When you combine them, it shortens recovery time," says Radford. "And when you add a growth factor it further shortens recovery. Bone marrow engraftment usually takes about three weeks. In this study it's only taking about eight days. That's important because transplant patients are extremely vulnerable to infection until engraftment. That's when most of the morbidity and mortality

Dr. James Radford is investigator for the University's participation in a new nationwide trial of bone marrow transplantation.



associated with bone marrow transplants happens. The mortality rate with this trial is about 5 percent. Typically the rate is about 15 percent. And patients only need to be in the hospital for three or four weeks instead of the usual six or eight weeks. I suspect that very soon most bone marrow transplants are going to be done this way."

Stephanie Daniels entered the bone marrow transplant unit on August 29 and was discharged on September 26.

"When I was in the hospital I felt tired, and lonesome for my children, but I didn't feel that sick," she says. "The worst part was actually having the bone marrow infused. It felt burning hot as it went into my vein. And it gave me an awful taste in my mouth. But they did it fast, and when it was done I felt fine."

Daniels' white blood cell counts were up to normal seven days after her transplant. It took several months, however, for her energy level to return to normal. Radford attributes her fatigue to chemotherapy, radiation therapy, and reduced thyroid function, which was a side effect of radiation she received before coming to UMHC. Typically, Radford says, it takes patients three to four months to get back to a normal energy level. During her recovery period Daniels was hospitalized for a few days when she developed

Dr. Phillip McGlave is director of the Medical School's adult bone marrow transplant program.

shingles, a common side effect of bone marrow transplantation.

"It was all worth it," she says. "In about February, my energy came back with a whoosh. And by spring I could do it all—play with the kids, ride my bicycle, garden, and mow the lawn."

A new approach

About 340 women will be enrolled in the trial nationwide. Radford hopes to enroll 30 at the University of Minnesota. Because of the trial's low mortality rate, a spinoff protocol for women with stage II breast cancer and only four to nine positive lymph nodes is being developed by the CALGB. Meanwhile, Radford and McGlave are putting together their own protocol for women with advanced (stage IV) breast cancer.

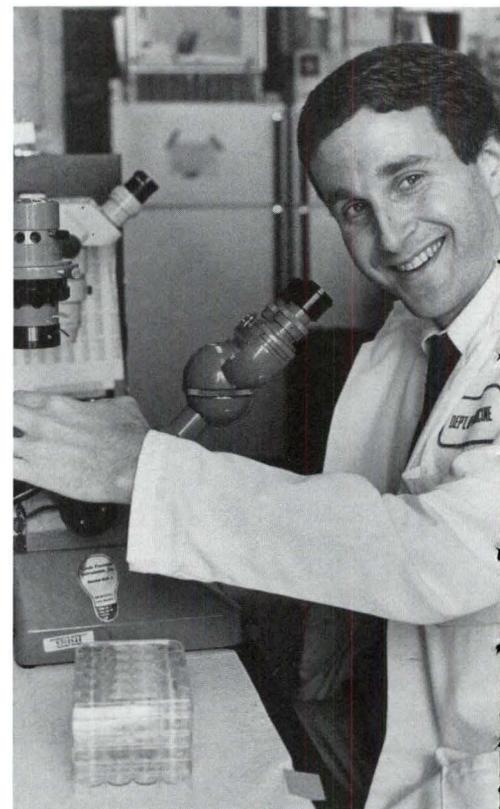
"This is a larger group of women with a poorer prognosis. We have several studies on the drawing board and expect to be ready to begin clinical trials in the next six to twelve months," McGlave says.

Bone marrow transplantation hasn't worked very well for advanced breast cancer. Eighty percent relapse within two

years after their transplants, probably because breast cancer cells have invaded their bone marrow, according to McGlave. He plans to use a new approach to select healthy stem cells from other marrow cells based on their size, density, and surface receptors. The technique was developed by Catherine Verfaillie, assistant professor of medicine, and McGlave.

"We think this will give us a pure population of stem cells to start up the bone marrow after high dose chemotherapy," he says. McGlave and his colleagues are pioneering several techniques to select populations of benign cells from bone marrow.

While the majority of women with advanced breast cancer relapse after transplant, nearly all are in remission for a short time. McGlave and Radford see this time as a window of opportunity to give immunotherapy to eliminate the residual cancer cells that cause relapse. They plan to use a combination of interleukin-2 and natural killer cells developed by Jeff Miller, assistant professor of



Dr. Jeff Miller developed a program of immunotherapy to eliminate residual cancer cells that cause relapse.

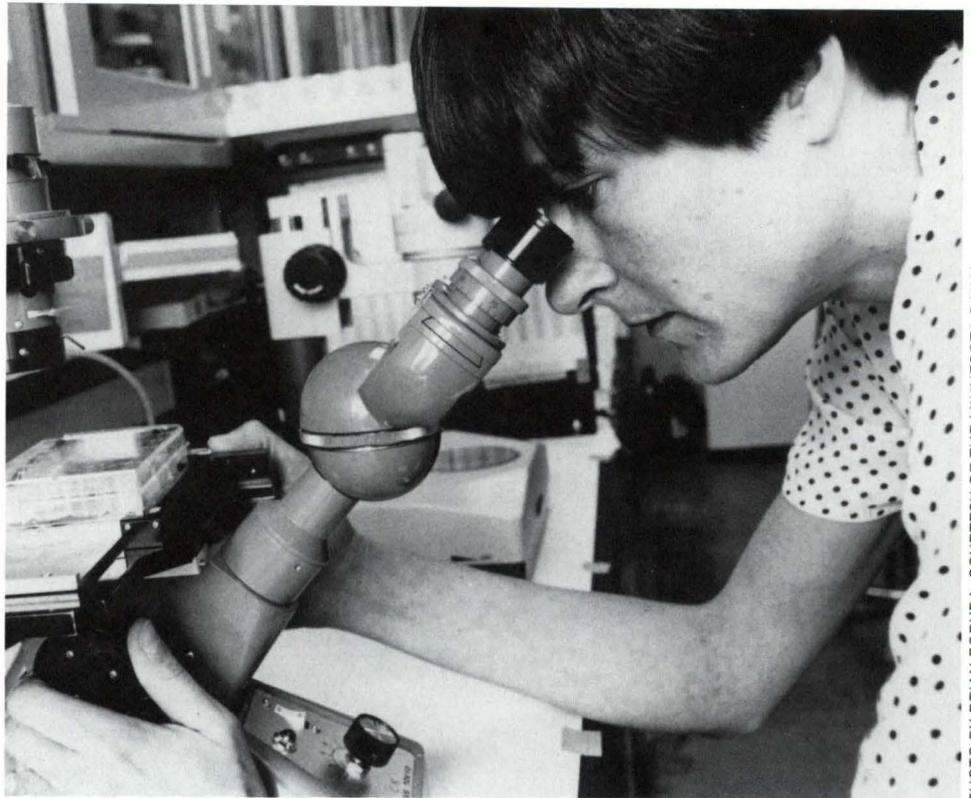
medicine.

If the results of trials of bone marrow transplantation for breast cancer are positive, trials for other solid tumors are expected to follow. Small cell lung cancer and ovarian cancer may be next because, like breast cancer, they are very sensitive to chemotherapy. McGlave foresees other changes in the field. Bone marrow transplantation has been considered a therapy of last resort because it is intense and risky. New techniques to accelerate production of red and white blood cells after transplantation are reducing the risk, and more ways to make transplantation better and safer will undoubtedly follow. The changes are happening so quickly it may not be long before bone marrow transplants can be given on an outpatient basis. In fact, McGlave has begun working with UMHC administration on a plan for a comprehensive outpatient bone marrow facility.

"Inpatient care would only be necessary for high dose chemotherapy and radiation, and bone marrow infusion. Patients could go home much sooner," McGlave says. "We could give some of these innovative treatments, like immunotherapy, as well as more routine things, like transfusions and antibiotic therapy, on an outpatient basis. This would be particularly appropriate for patients being treated for breast cancer and other solid tumors. We want to pioneer outpatient therapy for bone marrow transplantation here, and the hospital is very receptive."

The bone marrow transplantation program at the University of Minnesota was the first of its kind and is now the second largest in the world. Basic and clinical researchers in the program are looked to as leaders in developing innovations that advance the field. The first successful allogeneic (donor) bone marrow transplant was done here in 1968. During the 1970s John Kersey, who is overall director of the University bone marrow transplantation program, Norma Ramsay, director of pediatric bone marrow transplantation, and colleagues conducted large-scale trials showing that matched sibling bone marrow transplants are effective therapy for a variety of otherwise fatal diseases, including leukemia and aplastic anemia.

The shortcoming of donor transplantation is that many patients can't be



Dr. Catherine Verfaillie has developed a new process for cultivating mature blood cells from stem cells in the laboratory.

matched with a donor. So in the late 1970s and early 1980s University researchers began to look at autologous transplantation. Kersey, Daniel Vallera, professor of therapeutic radiology, and Fatih Uckun, associate professor of therapeutic radiology, developed immunotoxins to clear the marrow of cancer cells before returning it to the patient. An immunotoxin is a monoclonal antibody that recognizes a particular type of cancer cell fused with a toxic protein that kills cancer cells. The approach has been used primarily to treat acute lymphocytic leukemia, the most common form of leukemia in children.

McGlave has recently turned his attention to the flipside of purging cancer cells from bone marrow—selecting populations of healthy stem cells. In a recent issue of *Blood* he and Verfaillie published results of a study showing how healthy stem cells could be selected from the marrow of patients with chronic myelogenous leukemia based on differences in their size, density, and cell-surface receptors. Theoretically, the benign stem cells could be reinfused into the patient after high-dose chemotherapy and radiation to reestablish the marrow.

"If we can make this approach work in chronic myelogenous leukemia, we can

apply it to the treatment of other cancers that invade the bone marrow," says McGlave. "We hope to develop a generic test to select healthy stem cells from bone marrow that has been invaded by any type of cancer."

Verfaillie has recently developed a process for cultivating mature blood cells from stem cells in the laboratory. McGlave expects the technique to have multiple applications for bone marrow transplantation. By combining benign stem cells selected from bone marrow and cultivated mature blood cells engraftment would be shortened and the need for transfusions reduced. Additionally, the method would make it possible for patients with only a few benign stem cells remaining in their bone marrow to have autologous transplants.

McGlave predicts that refinement of bone marrow transplantation will continue over the next few years, and that gene therapy may be used in combination with bone marrow transplantation. Ultimately, he thinks, bone marrow transplantation will become safe, quick, and cost-effective, and will be widely used to treat many forms of cancer as well as congenital disorders that affect the bone marrow.

Peggy Rinard is a science writer for the University of Minnesota office of Health Sciences Public Relations.

A gift repaid

Dr. William Knobloch is repaying the generosity that was shown to him as a student by supporting education and research at the Medical School.

by Elaine Cunningham

Dr. William Knobloch remembers what it was like to be a medical student, struggling to make it through school. He knows what it was like to hold multiple jobs and still worry about paying his next quarter's tuition. He remembers the hard work of those days.

But Knobloch also remembers the kindness and generosity of those who helped him in medical school. It is that generosity that he seeks to repay. It is why he has established the Knobloch Medical Student Scholarship Fund through the Minnesota Medical Foundation which will provide two annual four-year renewable scholarships.

The first two students to receive Knobloch Scholarships are Thomas W. Frederickson and Lora L. Truckenbrod. Each year, a male and female student from the entering class will be selected to receive Knobloch Scholarships and, providing they remain eligible, they may renew their scholarships annually for the next three years. Thus, by 1994, eight Knobloch scholarships of approximately \$1,500 each will be awarded.

Supporting medical students is important to Knobloch, a professor of ophthalmology and interim head of the Department of Ophthalmology, because of his own experiences in medical school. When he began classes at the University of Oklahoma School of Medicine in 1948, he was an older student. He had already served in the Navy during World War II, he was married to his first wife Vel, and he had one child. Two more children would be born before he graduated.

"There were no scholarships or loans available back then," Knobloch recalls. "The G.I. Bill paid for some of my schooling, but I had to work about 25 hours a week to pay for the rest and support my family."

Knobloch held a number of odd jobs,

THE KNOBLOCH SCHOLARSHIP RECIPIENTS

Lora Truckenbrod grew up in Selma, California. Her father is a minister, her mother a teacher, and she has four siblings. She graduated from California Lutheran University with a degree in biochemistry. She chose medicine as a career because, she explains, it is a "helping profession" and she has always enjoyed helping others. Although she has not yet selected a speciality, she is leaning toward internal medicine. So far she really likes it at the University of Minnesota Medical School because "the students are supportive and helpful of each other."

Tom Frederickson decided to enter

medical school after several years in the business world. He received an MBA from the University of Indiana and got a position with Proctor & Gamble in Cincinnati. His undergraduate degree in history and Spanish came from Brigham Young University. He decided, however, that medicine, not business, was his career choice, and he plans to specialize in family practice. Tom is married and has three children, and says the Knobloch Scholarship will be "really helpful." He is also working as a research assistant in the Department of the History of Medicine to help make ends meet.



The first two students to receive Knobloch Scholarships are Tom Frederickson, left, and Lora Truckenbrod, right. Dr. Knobloch and his wife, Donna Irlbeck, greeted the students at the MMF Spring Awards Reception.

from washing laboratory equipment to mowing lawns. He worked as much as he could and sometimes that was not enough. Many people helped him out. The biochemist whose lab he worked in loaned him money on several occasions. Once, a family friend came by the house during a particularly desperate time and gave Vel \$100. His reason was simply that he'd been thinking about them and realized that times must be difficult.

One act of generosity that Knobloch remembers came during his three-month preceptorship in a small town. Because of the preceptorship, he was unable to work at his jobs back at school. In addition, his eldest daughter had just been released from the hospital after a bout with polio, and there was a new baby at home which meant his wife was unable to work.

"I didn't know how I was going to pay my next quarter's tuition," he says now, "but I had faith that something would happen." His faith was upheld when the small town doctor he was working with wrote him a check for \$500, telling him it was for his medical education.

"I told him I didn't know when I'd be able to pay him back," Knobloch recalls. "He said he didn't expect to be repaid."

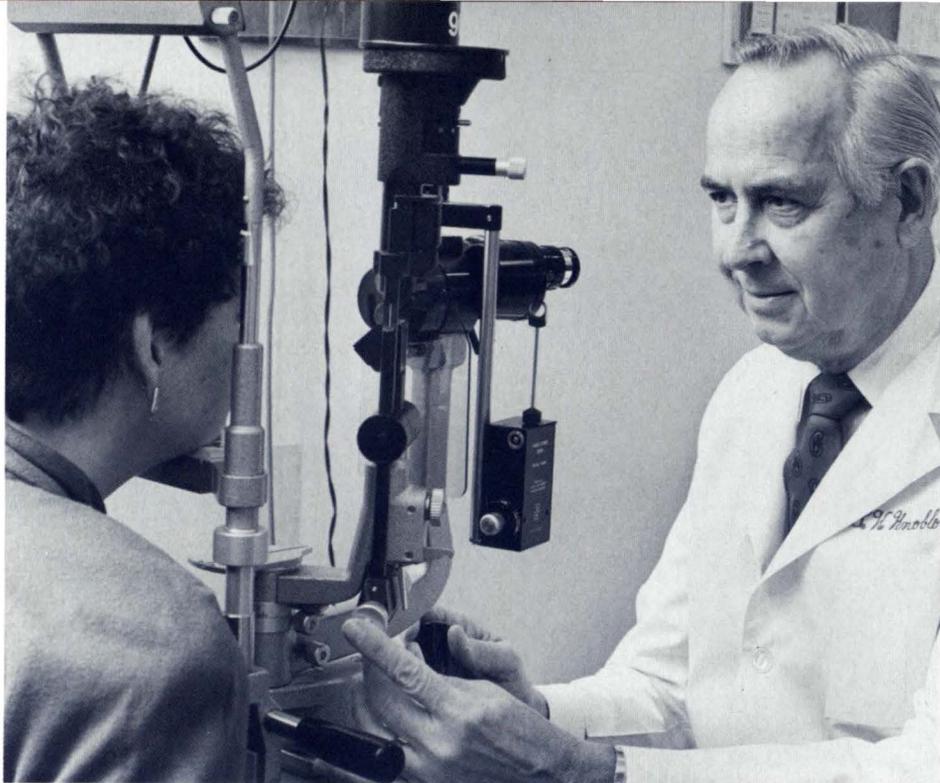
Choosing a life of service

Through the Knobloch Scholarship Fund, however, Knobloch has found a way to pay back that debt as well as all the other acts of generosity.

"I was always intrigued by science," says Knobloch, "and I felt drawn to medicine because it was a profession of service. All the acts of generosity I experienced in medical school reaffirmed my belief that going into medicine was the right thing for me to do."

To the patients, students, residents, and staff at the University of Minnesota whose lives have been enriched by Knobloch's skills as a physician and teacher, his choice of medicine was most certainly the correct one.

Knobloch joined the ophthalmology faculty at the University of Minnesota as an assistant professor in 1964. Prior to that he had spent several years in family practice, followed by a retinal fellowship in St. Louis. At the time, there was no specialist for surgery and diseases of the retina at Minnesota. Knobloch became one of the first retinal specialists in the Upper Midwest and built an extremely active practice. By 1968, he was operating on 500 to 600 retinal detachment patients each year.



Dr. William Knobloch's pioneering work in the genetic aspects of eye diseases resulted in the establishment of the University's Genetic Eye Clinic.

"It was a very busy time," Knobloch says. "Detached retina was the second leading cause of hospitalization at the University of Minnesota in those years. I worked hard and the residents worked hard." To date, Knobloch has operated on more than 8,000 eyes with retinal detachments and trained 160 residents and eight fellows.

Patient care and resident education, Knobloch believes, are the two most important aspects of his vocation.

"The thrust for doctors is patient care, given with kindness and caring," he explains. "The patients' interests should come first. Residents learn from us as teachers. The best education is showing residents exemplary patient care."

A research pioneer

Concern about enhancing patient care led Knobloch to become involved in clinical research activities. His funded research activities have brought in more than \$2.5 million to the University of Minnesota Medical School and resulted in numerous advances. His areas of study have included inherited vitreoretinal degenerations, ocular findings in twins reared apart, retinal detachment surgery, diabetic retinopathy, silicone vitreous replacement, and retinopathy of prematurity.

His pioneering work in the genetic aspects of eye diseases resulted in the establishment of the University's Genetic Eye Clinic. As part of this clinical research activity, Knobloch also made a

discovery about retinal detachment and encephalocele that is now referred to as the Knobloch Syndrome. His interest in new syndromes continues with current investigations of families with inherited vitreoretinal degenerations.

Knobloch's interests in clinical research and education led to his establishing yet another fund through the Minnesota Medical Foundation—the Knobloch Retina Research and Education Fund. He hopes as this fund grows it can have a significant impact on furthering research, training, and surgery in the diseases of the retina.

As his career has flourished, Knobloch has never forgotten the financial difficulties he and his family encountered during his medical school days. Following the death of Vel Knobloch in 1987, the Knobloch Medical Student Scholarship Fund was established.

"I felt that using the memorial gifts given in her honor for medical student scholarships was appropriate since she had experienced the hardships of medical school with me," he says.

During the past few years, the fund has steadily grown with contributions from Knobloch, his wife Donna Irlbeck, their friends and colleagues. The generosity of others lightened some of the financial burden for Knobloch, allowing him to concentrate on his studies. The continued growth of the Knobloch Scholarship Fund will lighten this burden for medical students far into the future.

Rowers

The Memorial Day Regatta supports

pull for

leukemia research at the University of

leukemia

Minnesota Medical School.

by Jean Murray

The 33rd Annual Memorial Day Regatta-1992 Midwest Rowing Championships, held May 24 at St. Paul's Lake Phalen, was not just an exciting sporting event. The more than 400 rowers from the Midwest and Canada were also participants in the fight to find a cure for leukemia.

Hosted by the Minnesota Boat Club (MBC)—which at age 122 is the state's oldest athletic institution—the event is sanctioned by the United States Rowing Association, with champions qualifying for the U.S. Elite Nationals.

This is the third consecutive year that the Memorial Day Regatta has supported leukemia research at the University of Minnesota Medical School through the Minnesota Medical Foundation (MMF). Proceeds come from T-shirt, poster, and advertising sales, as well as from private donations.

Dr. Charlene McEvoy, president of the Minnesota Boat Club, says, "Rowing has enriched the lives of our athletes. Throughout the years, MBC has enjoyed the support of the community; now we feel it is our turn to reciprocate. In association with MMF and the University of Minnesota Internal Medicine Residents' Council (UMIMRC), the Memorial Day Regatta once again has been utilized as a fund raiser for leukemia research. Inspiration for this idea comes from the unfortunate fact that three of our members have been stricken with this disease."

The fund at the Minnesota Medical Foundation has been renamed this year, memorializing rower Jim Woog, who died of leukemia in February. It is now called the James N. Woog Pull Together for Leukemia Fund. All proceeds from the Regatta go to leukemia research at the University, with no expenses or administrative fees taken out.

Leukemia research underway

The Minnesota Medical Foundation is actively involved in the fight against leukemia. The following grants were given recently by MMF to Medical School researchers who are working to find a cure for this disease which touches children and adults alike.

Dr. Fatih M. Uckun, associate professor in the Department of Therapeutic Radiology and director of the Section of Cancer and Leukemic Biology, received \$15,000 from MMF to support his project entitled "Molecular immunology studies." He initially described his project as follows: "These studies are designed to clone the genes for novel surface receptors of lymphoid progenitor cells. Their regulation in normal and leukemic cells will be analyzed and compared. The information from these studies may lead to therapeutic innovation in human leukemias."

In summarizing the results after the study was completed, Uckun says, "We





Robert Burgett, MMF's associate vice president of development, receives a donation of \$250 from the St. Paul fire fighters, who served as the emergency team at the Regatta.



have used molecular techniques to study the signaling events in human lymphocytes and lymphocyte precursors stimulated with various cytokines and growth regulatory reagents. The results of our studies have expanded our knowledge regarding the basic immunology in human lymphocyte development and function."

Uckun describes how the research project has contributed to the advancement of medical science by saying, "The molecular analyses performed under this grant have improved our understanding of the leukemia cell biology. The results obtained have provided the basis for new attempts to design more effective therapeutic strategies for the treatment of human cancer. We now have a better understanding as to how best to control the cancer cell growth in the human body."

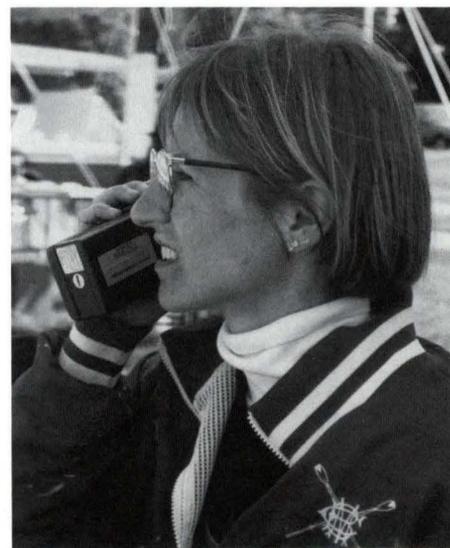
Dr. Catherine M. Verfaillie, assistant professor in the Department of Medicine, received \$20,000 from MMF for her study of "Receptors for adhesion of human hematopoietic cells to fibronectin." She says, "Fibronectin is an important molecule in different organs that secures correct alignment between different cell types. We have demonstrated that human primitive bone marrow (BM) cells, which can generate more mature blood cells for several months when cultured under appropriate conditions, bind to fibronectin.

"We propose studies to characterize the receptors on primitive BM cells responsi-



ble for this interaction, including experiments where binding of primitive BM cells to fibronectin is prevented by different soluble molecules, followed by experiments in which these receptors are extracted from the BM cells and their composition characterized. These studies will help explain why primitive BM cells remain in the BM cavity and why BM cells infused into patients during a BM transplantation bind specifically to the BM cavity."

Dr. John E. Wagner, assistant professor in the Department of Pediatrics, received \$15,000 from MMF for his project entitled "Characterization of the graft-vs-leukemia effect." He explains his research by saying, "Although there have been significant advances in the treatment of patients with leukemia, the long-term leukemia-free survival is poor. In an



Dr. Charlene McEvoy is president of the Minnesota Boat Club.

attempt to increase the number of patients who are cured of this disease, the role of bone marrow transplantation in the treatment of leukemia has been investigated.

"Bone marrow transplantation decreases the risk of leukemia relapse in two ways: 1) it enables the patient to receive higher doses of chemotherapy than would ordinarily be possible, thus eradicating more leukemia cells, and 2) it has an anti-leukemia effect of its own, referred to as "graft-vs-leukemia." It is believed that immune cells in the bone marrow of a normal donor recognize and react with leukemia cells that have survived the chemotherapy. In much the same way that an individual's system can reject a transplanted kidney or heart, it is believed that immune cells in the donated bone marrow (which are not present in donated kidneys or hearts) can reject leukemia cells.

"The purpose of this project is to identify and characterize the cell(s) responsible for this anti-leukemia effect of normal bone marrow. If the cell(s) can be identified first in an animal model, perhaps we can find these cells in human bone marrow and manipulate them in such a way as to accentuate their ability to kill the leukemia cells remaining after high-dose chemotherapy."

Dr. John C. Winkelmann, assistant professor in the Department of Medicine and the Institute of Human Genetics, received \$4,000 from MMF for his research on "The human erythropoietin receptor." He explains, "Erythropoietin (Epo) is a hormone that regulates the physiological production of red blood cells. It has also emerged as an important therapeutic agent in the treatment of anemias.

"Yet, little is known of the mechanism of Epo action. Its effects at the cellular level are initiated by its association with a specific cell surface receptor. The human erythropoietin receptor (EpoR) is of particular interest to investigators interested in normal and pathological red cell production, including diseases such as pure red cell aplasia, polycythemia vera, and erythroleukemia.

"The proposed project uses the techniques of molecular and cellular biology to investigate the structure, function, and expression of the human EpoR. It is anticipated that the results of these experiments will enhance our basic understanding of the normal and pathological production of red blood cells."



Nearly \$26 million has now been pledged in the \$30 million campaign to establish the University of Minnesota Cancer Center. Proceeds will be used to: build a 78,000-square-foot state-of-the-art research facility that will provide much-needed laboratory, seminar, and office space; establish at least eight endowed chairs to attract leading cancer experts who will supplement an already outstanding group of researchers; and provide funding for new research programs and expansion of existing programs.

Planning is moving forward on construction of the new facility. Architectural plans are being refined and space utilization plans are being updated in anticipation of construction beginning in early 1993.

The Cancer Center will serve as the focal point of the University of Minnesota's far-reaching effort to intensify and expand research into the causes, diagnosis, treatment, prevention, and cure of cancer.

The Masonic Cancer Center Fund, Inc. has increased its pledge to the University of Minnesota Cancer Center from \$2 million to \$5 million. In recognition of this extraordinary commitment, the new research facility will be named the Masonic Cancer Research Building. On April 23, at the Annual Meeting of the Minnesota Masons, a large pledge card representing the gift was presented to University President Nils Hasselmo and Cancer Center campaign General Chair

Winston Wallin by Mrs. Dorothy "Tudy" Motschenbacher, president of the board of directors of the Masonic Cancer Center Fund, Inc. Accepting the pledge card from Mrs. Dorothy "Tudy" Motschenbacher, president of the Masonic Cancer Center Fund, Inc. board of directors, is University of Minnesota President Nils Hasselmo and Cancer Center campaign General Chair Winston Wallin.

Winston Wallin by Mrs. Dorothy "Tudy" Motschenbacher, president of the board of directors of the Masonic Cancer Center Fund, Inc.

Further highlights include: pledges and gifts totalling \$6.2 million from University of Minnesota Medical School and Health Sciences faculty, underscoring exceptional commitment to the effort; a combined total of \$250,000 pledged by three donors toward an endowed chair in women's cancer research, a drive chaired by Emily Anne Staples; and four endowed chairs either pledged or funded in the areas of children's cancers, breast cancer, bone marrow transplantation, and cancer prevention and genetics. Each chair will serve to attract preeminent cancer experts whose research will complement the University of Minnesota's already extensive cancer research and patient care program.

For more information on how you can help support the University of Minnesota Cancer Center, call Mark Zachary at (612) 625-4441.

MEDICAL SCHOOL NEWSBRIEFS

Anesthesiology

Dr. Joseph J. Buckley, professor emeritus, received the 1992 Citation of Merit from the Academy of Anesthesiology "in recognition of his outstanding and devoted talents as a teacher and administrator, recently evidenced by the establishment by his former students of the J.J. Buckley Research Fellowship; his long continuing academic promotion of the specialty of anesthesiology; his many contributions in advancing the science of anesthesiology, especially in the areas of acid-base physiology, hypothermia, and organ transplantation; his warm friendly personality which is extended to all; and his outstanding and efficient services as secretary of the Academy of Anesthesiology for ten years."

Department head Dr. Richard J. Palahniuk was the invited lecturer at the International Anesthesia Research Society. Dr. Ian J. Gilmour, assistant professor, was appointed a new member of the Minnesota Respiratory Care Practitioner Advisory Council for 1992 to 1996. Faculty changes within the department include the appointment of Dr. Barbara S. Gold as assistant professor and the retirement of associate professor Dr. James F. Cumming.

Assistant professor Dr. Scott Augustine, founder and CEO of Augustine Medical, Inc. of Eden Prairie and inventor of the Bair Hugger Patient Warming System, accepted the 1992 award for "Outstanding Achievement in a Health Care Product" given to the company by the Medical Alley Association. The award cited the warming system as an innovative solution for controlling hypothermia.

Biochemistry

Dr. Michel M. Sanders has been promoted to associate professor, and Dr. Brian G. Van Ness has been promoted to professor.

Research grants recently received in the department include: Dr. James B. Howard, NSF, Site-Specific Mutation of Nitrogenase Proteins, \$321,000; Dr. James F. Koerner, NIH, Glutamate Analogues on Hippocampal Neurons, \$276,214; Dr. John D.

Lipscomb, AMOCO, Structure and Chemistry of Catalysts for Oxidative Hydrocarbon Conversions, \$45,000; Dr. James Mahaney, NIH, Transient Spectroscopy of Muscle, \$700,952; Dr. Douglas H. Ohlendorf, NIH, Structural Studies of Dioxygenases, \$376,589; Dr. Howard C. Towle, NIH, Nutritional and Hormonal Regulation of Hepatic Genes, \$574,221; and Dr. Brian G. Van Ness, NIH, Rearrangement and Regulation of Immunoglobulin Genes, \$388,555.

Dermatology

Dr. Sergei Grando has joined the department as associate professor. He is an internationally known dermatologic research worker from Kiev, Ukraine, specializing in the pathogenesis of immunobullous disease.

Laboratory Medicine and Pathology

Dr. Karen Lofsness, assistant professor, has received the Morse-Alumni Award for Outstanding Contributions to Undergraduate Education from the Minnesota Alumni Association and the University of Minnesota.

Medical Technology

Dr. Karen Karni, associate professor of Laboratory Medicine and Pathology and director of the Division of Medical Technology, was presented with the Robin H. Mendelson Memorial Award at the 1991 American Society for Medical Technology Annual Meeting. The award honors outstanding service and contributions to the profession. Karni also was recently selected to receive the Minnesota Society for Medical Technology Service Award for her excellent service to the state organization.

Medicine

Dr. Dale Hammerschmidt, associate professor and senior editor of the *Journal of Laboratory and Clinical Medicine*, was elected to the Minnesota Tourette Syndrome Association's board of directors in February. Dr. Louis Tobian, professor,

received the Richard Bright Award from the American Society of Hypertension in May. The award recognizes pioneers in nephrology.

Obstetrics and Gynecology

New residents in the department include Drs. Rebecca F. Burton, Diana N. Contreras, Laura A. Dean, Christie A. Iverson, Manhot Lau, John C. Nadeau, and Kathryn M. Nelson. New fellows include Drs. Ellen Hartenbach and Andrew K. Saltzman.

Ophthalmology

Dr. Jonathan Wirtschafter will be the principal investigator on the new Traumatic Optic Neuropathy Pilot Project. Dr. Robert Letson recently spent a month working at the United Methodist Church Eye Hospital in FreeTown, Sierra Leone, West Africa. Dr. Malcolm McCannel was awarded the Ophthalmology Department Vision Foundation's Alumni Service Award in December for his positive influence on the department for 50 years.

Pediatrics

Dr. David E. Fisher was named associate professor of pediatrics and head of pediatrics at Hennepin County Medical Center. Grants received by department members include: Dr. Michael Mauer, \$49,000 for Renal auto-regulation in diabetes; Drs. John Wagner and John Kersey, \$32,000 for Characterization of bone marrow cell population; Dr. Robert Blum, \$54,000 for Needs assessment of parents; Dr. Mary Kleppel, \$44,000 for Characterization of novel 55KDA basement membrane molecules; and Drs. Kim Krabill and Al Rocchini, \$24,000 for Use of stents in aortal coarctation. Dr. John Perentesis was named University Children's Foundation Scholar, and department head Dr. Alfred F. Michael is president elect of the American Society of Nephrology.

Pharmacology

Dr. Daniel Romero has been named assistant professor. Grants received by depart-

ment members include: **Dr. Stanley A. Thayer**, an NIDA grant for HIV-1 Neurotoxicity: Mechanism and Modulation by Opioids; and **Dr. Ben G. Zimmerman**, an Upjohn grant for Blockade of Local Angiotensin Production. **Dr. Akira E. Takemori** will assume presidency of the American Society for Pharmacology and Experimental Therapeutics on July 1.

Radiology

Dr. Robert J. Boudreau has been appointed president elect for the Central Chapter of the Society for Nuclear Medicine. **Dr. Wilfrido Castaneda** headed the Third International Course on Vascular and Interventional Radiology as the Therapeutic Alternative in the Canary Islands, Spain. **Dr. Deborah Day** won the Society of Gastrointestinal Radiology Research Award for 1992 for the "Doppler evaluation of pediatric bone marrow transplant patients as an aid in early diagnosis of hepatic veno-occlusive disease." She is also president elect of the Minnesota Radiology Society. **Dr. Christopher E. Engeler** recently presented a paper on "The insertion of Gelfoam plugs after lung biopsy" at the Thoracic Society Meeting in Laguna Niguel, which will be published soon in *Radiology*.

Drs. David E. Finlay, Janis Letourneau, and Deborah Longley received the Cum Laude award from the Radiological Society of North America (RSNA) for an exhibit entitled "Vascular assessment of the kidney, liver, and pancreas transplant recipient." **Dr. Mary C. Foshager** is joining the faculty as assistant professor in ultrasound. **Dr. Harry J. Griffiths** presented a paper on the "Complications of Long Bone Allografts" at the Society of Skeletal Radiology in Phoenix, where he was also made co-chairman of the Academic Committee. **Dr. Christopher C. Kuni** received a Certificate of Merit from the RSNA for an exhibit on "Failure of hypoxic vasoconstriction response in single lung transplants."

Department head **Dr. William M. Thompson** is the new secretary-treasurer for the Society of GI Radiologists. **Dr. James W. Walsh** is co-investigator on two phase-2 trials of contrast media in MRI, and has been appointed president

of the Society of Computed Body Tomography.

Therapeutic Radiology

Dr. Seymour Levitt, professor and head of the department, was elected to a six-year term on the Radiological Society of North America Board of Directors. **Dr. Fatih Uckun**, associate professor, was selected by the Leukemia Society of America as a Stohlman Scholar for 1992. The award recognizes the most creative and productive members of the society.

School of Public Health

Dr. Stephen Joseph, dean of the School of Public Health, received the 1992 Outstanding U.S. Alumnus Award for Public Health Leadership from Johns Hopkins University. He was also elected to membership in the Johns Hopkins Society of Scholars. The association honors distinguished postdoctoral fellows of that university.

The M.D./Ph.D. Program

The first M.D./Ph.D. Student Sponsored Lecture Series presentation was held March 10. Featured lecturer was Dr. Michael Blaese of the National Institutes of Health, speaking on Progress in Gene Therapy. According to the mission statement, the Combined M.D./Ph.D. Student Sponsored Lecture Series constitutes an offering from the students to the greater University community. The series provides a means to help define the role of the physician/scientist in clinical medicine, in basic research, and in the world. As a student initiated program, it provides for an active role on the part of the students to create and express a vision of what medical science can offer.

MMF approves \$122,835 in research grants

The Minnesota Medical Foundation board of trustees approved \$122,835 in research and special grants at its winter quarterly meeting. The amount includes \$48,700 in faculty research grants, \$9,000 in student research grants, and \$65,135 in special grants for research equipment and salary support.

Faculty grants include: **Joseph Di Salvo, Ph.D.**, Physiology, UMD, \$6,000, Modulation of excitation-contraction coupling in vascular smooth muscle; **Timothy J. Ebner, M.D., Ph.D.**, Neurosurgery, \$4,000, Optical recording of digit representation in the monkey somatosensory cortex using voltage sensitive dyes; **John E. Folker M.D., Ph.D.**, Surgery, \$5,000, Energy metabolism in the immature myocardium; **Beulah Holmes Gray, Ph.D.**, Microbiology, \$9,000, Adult respiratory distress syndrome: studies of the role of Proteinase 3; **Matt G. Kushner, Ph.D.**, Psychiatry, \$5,000, Ethanol's effect on CO₂ induced panic and anticipatory anxiety: a double-blind balanced placebo evaluation; **Arthur J. Matas, M.D.**, Surgery, \$3,700, Clonal anergy in organ transplantation; **Martha A. Nance, M.D.**, Neurology, \$5,000, New approaches to the study of hereditary ataxia: clinical and psychosocial assessment; **Mark Rosenberg, M.D.**, Medicine, \$8,000, Clusterin and renal injury; and **Peter A. Santi, Ph.D.**, Otolaryngology, \$3,000, An immunohistochemical investigation of inner ear antigens using antibodies produced by patients with Meniere's disease.

Student grants, at \$1,800 each, include: **Irene V. Pech**, Year 4, Factors predicting response to therapy for graft versus host disease in bone marrow transplant patients; **Kevin M. Coonan**, Year 3, Erythromycin resistance in pathogenic streptococci; **Joseph W. Leach**, Year 3, Will 15-deoxyspergualine suppress rejection of guinea pig to rat corneal xenografts?; **Michael Stenzel**, Year 4, The role of cellular infiltration in the development of irreversible renal injury following chronic ureteral obstruction; and **John W. Cromwell**, Year 3, Construction

Continued on page 20

MMF Grant Recipient: Dr. Bruce Hammer

Bruce Eric Hammer, Ph.D., assistant professor in the Department of Radiology, was one of 16 faculty members to receive a grant at the Minnesota Medical Foundation's winter meeting of the board of trustees. In all, the MMF board approved \$122,835 in faculty research grants, student research grants, and special grants (see adjacent article.)

Hammer received \$10,000 in support of his project entitled "Nuclear Magnetic Resonance Imaging of Flow and Metabolites in Hollow Fiber Bioreactors."

In describing his project, Hammer says, "Bioreactors are devices engineered to maintain an optimal environment for cells from which biochemically synthesized products, such as insulin or antibodies, are harvested. These devices are also being developed to function as artificial organs. One example is an artificial liver being developed in the Departments of Surgery and Chemical Engineering that is designed to temporarily maintain a patient with liver failure until a suitable liver donor is found.

"Nuclear Magnetic Resonance (NMR) spectroscopy/imaging technology will be used to non-invasively evaluate the performance of bioreactors by the spatial measurement of flow and cell metabolism. This should aid in obtaining optimal performance from existing bioreactors and help in the engineering and evaluation of new bioreactor designs."

Hammer explains that the specific type of bioreactor to be examined is known as a hollow fiber bioreactor (HFBR) which is principally used to grow mammalian cells. The core of the reactor consists of many hollow fiber membranes, the composition and porosity of which can be varied for different systems. Nutrient medium pumped into the hollow fiber is free to diffuse through the fiber wall to cells trapped between the fibers or residing in the fiber's spongy matrix. Desired biochemical products and waste diffuse back into



Dr. Bruce Hammer

the hollow fiber to be removed. Anchorage dependent cells traditionally reside on the surface of the fiber while non-anchorage dependent cells lie in the voids between hollow fibers. The operation of this device is similar to the body's circulation system where hollow fibers are analogous to capillaries that perfuse cells in the interstitial space.

"Cell viability in an operating bioreactor is controlled by a number of variables including pH, temperature, dissolved gases, cell density, and nutrient and waste concentrations," says Hammer. "If these parameters can be measured, control systems can be engineered that would maintain these cells in an optimal environment.

"NMR imaging has been successfully used to non-invasively view the internal structure of living organisms for well over 15 years," continues Hammer.

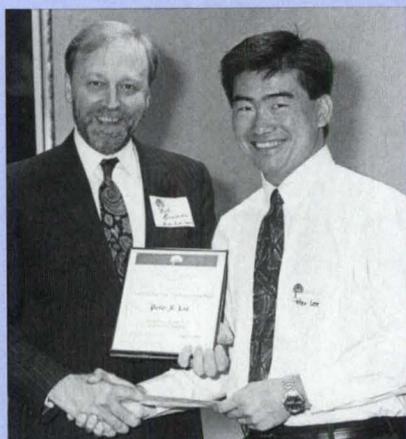
"This modality yields 3-D images without the use of hazardous ionizing radiation. This same technology can be applied to yield detailed pictures of the internal structure and function of HFBRs. NMR is the only noninvasive technique that can simultaneously measure cell metabolism, oxygen distribution, flow dynamics, and cell viability inside an operating HFBR."

Hammer received his Ph.D. in biomedical engineering from Northwestern University. He has been director of the Magnetic Resonance Section of Radiological Physics and assistant professor of radiology at the University of Minnesota since 1990. He was formerly manager of the Magnetic Resonance Research & Development Laboratory at Intermagnetics General Corporation in Guilderland, New York.

MMF announces award winners

The Minnesota Medical Foundation sponsors a number of awards throughout the year to honor the faculty and students of the University of Minnesota Medical Schools. The following awards and scholarships were recently awarded by MMF.

American Red Cross Award winner Peter Lee with Dr. Robert Bowman.



Cook Scholarship winner Jacalyn Dahl (left) with Thomas Cook and Dr. Richard Student, Nancy Bauer, and Thomas Hoban of the Hennepin County Medical Association Foundation.

American Red Cross Transfusion Sciences Research Award

Peter K. Lee
Recognizes exceptional research in transfusion medicine by an undergraduate medical student, a physician in postgraduate training, or a graduate student in the medical sciences.

Wallace D. Armstrong Memorial Award

Jeffrey J. Durr
Memorializes Dr. Armstrong, former chair of the Department of Biochemistry, by recognizing outstanding achievement in first year biochemistry.

John J. Bellomo, M.D., Outstanding Medical Student Award

Kevin J. Donnelly
Given by Mrs. Bellomo in memory of her husband.

Thomas P. Cook Scholarship

Jacalyn A. Dahl
Honors Mr. Cook, former executive director of the Hennepin County Medical Association Foundation.

Daniel A. Coyle Memorial Award

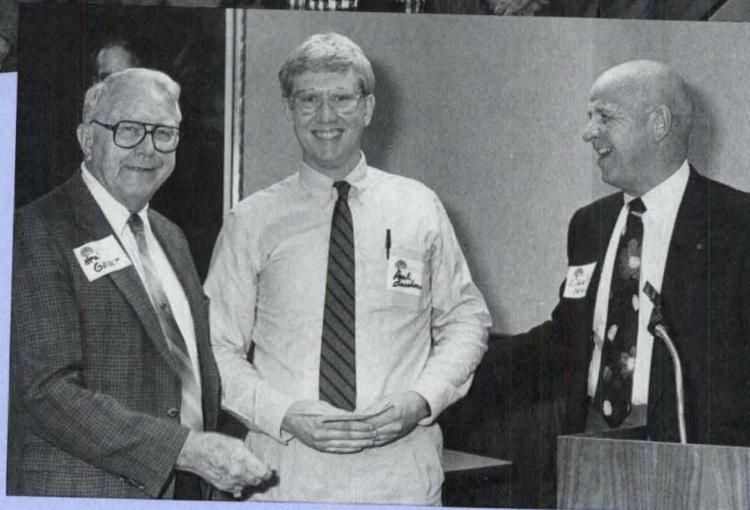
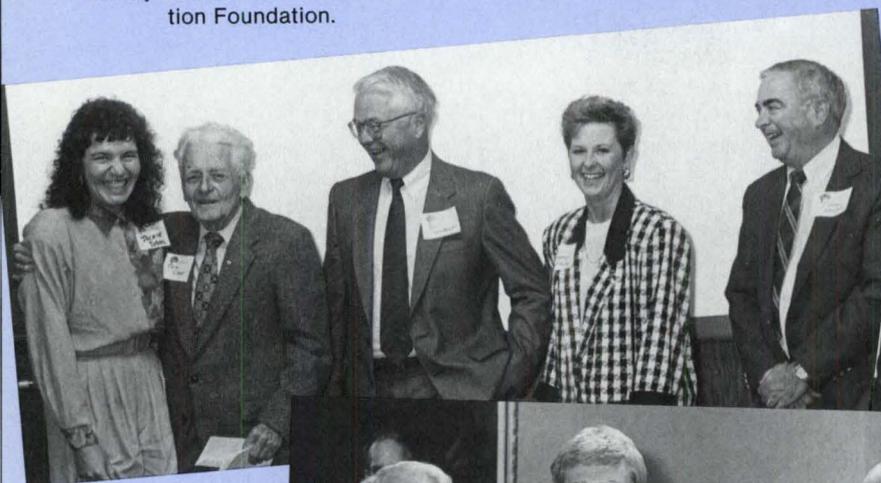
Rachel A. Bye
Honors an outstanding woman medical student in obstetrics and gynecology.

Dr. and Mrs. Stanley B. Crosbie Scholarship

Paul A. Jacobson
Established by Mrs. Crosbie in honor of the University of Minnesota Medical School, Dr. Crosbie's alma mater.

Dr. Luther Forest Davis Memorial Scholarship

George W. Leyda
Established in memory of Dr. Davis, a Wadena general practitioner, by his grandchildren.



Watson Award winners (from left) Frank Rimell, Gyorgy Balla, and Jon Jonsson.

Crosbie Scholarship winner Paul Jacobson with Dr. Neal Gault, Jr. and MMF President David Teslow.

Roger Dell Memorial Scholarships

Thomas R. Frerichs
Daniel A. Trajano
Funded by the Roger L. and Agnes C. Dell Charitable Trust.

Richard C. Horns Memorial Award

Mark A. Palmer
Memorializes Dr. Horns, professor of ophthalmology, by recognizing a senior medical student who has shown outstanding clinical promise.

Chester and Charlotte Johanson Scholarships

Allan F. Hunt
Steven J. Peckham
Established by Mr. Johanson in memory of his parents, Christine and Per Johanson, who were pioneer Traverse County, Minnesota, homesteaders.

Knobloch Scholarships

Thomas W. Frederickson
Lora L. Truckenbrod
Established as four-year renewable scholarships by William H. Knobloch, M.D., and his wife, Donna K. Irlbeck.

Lifson/Johnson Memorial Award

Lisa A. Carney
Established by the families, colleagues, and friends of Drs. Nathan Lifson and John A. Johnson, the award recognizes outstanding teaching by a graduate Student in the Department of Physiology.

J. Thomas Livermore Award

Kevin B. Urdahl
Established by Mr. and Mrs. Charles Livermore in memory of their son, the award recognizes outstanding original research in hematology.

Medical Student Achievement Awards

Deborah A. Dittberner
Joia S. Mukherjee
Beth A. Olsen
Minnesota Medical Foundation-funded awards which recognize graduating seniors who have excelled in student leadership, community service, academics, and research.

Metropolitan-Mount Sinai Outstanding Medical Student Awards

Curtis A. Meske
Joia S. Mukherjee
Established by the medical staff of the former Metropolitan-Mount Sinai Hospital as a remembrance and recognition of the contributions of that organization and its predecessors, the second- and fourth-year awards recognize students who show promise of becoming superior physicians or clinicians.

Mary Bizal Peterson Memorial Award

Rebecca D. Meyerson
Established by Dr. Edward Peterson in honor of his wife, the award recognizes a meritorious student embarking on a first year residency in neurology at the University of Minnesota Medical School.

R. C. Schneider Scholarship

Heather L. Hollender
Given by Mrs. R. C. Schneider in memory of her husband to honor University Hospital physicians and staff who provided special care for him.

Metropolitan-Mt. Sinai Award winners Curtis Meske and Joia Mukherjee with Dr. Joanne Rogin.

Undergraduate Research Awards

John D. Altman
Alan R. Hauser
Minnesota Medical Foundation-funded awards which recognize the most meritorious research paper written by a graduating senior.

Cecil J. Watson Awards

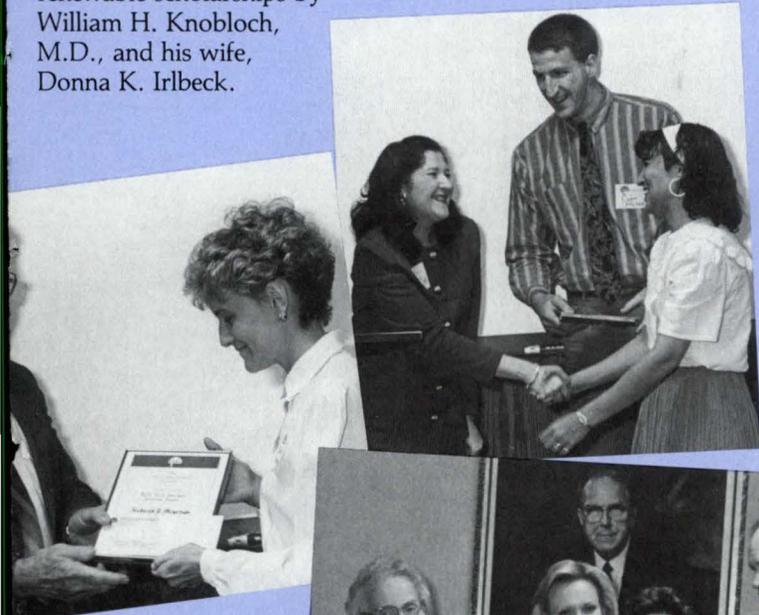
Gyorgy Balla
Jon J. Jonsson
Frank L. Rimell
Established in honor of Dr. Watson, Regents Professor of Medicine, the award recognizes outstanding research by a resident in clinical medicine.

George E. Williams Scholarship

Christopher N. Ta
Established in memory of Dr. Williams, former professor of psychiatry and assistant dean of student affairs.

Zagaria Research Award

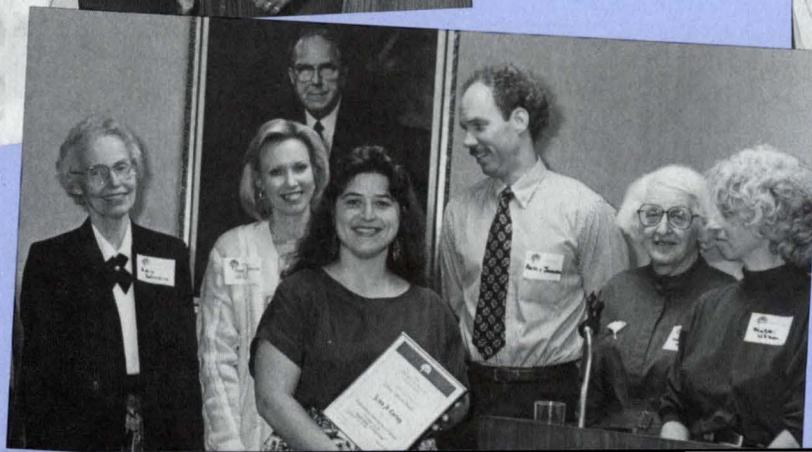
Christine M. Seroogy
Established to recognize original research in cardiology and oncology by an undergraduate.



Metropolitan-Mt. Sinai Award winner Rebecca Meyerson with Dr. Neal Gault, Jr.



Williams Scholarship winner Christopher Ta with MMF President David Teslow.



Lifson/Johnson Award winner Lisa Carney with (from left) Mrs. John A. Johnson, her daughter Peggy, and son Anton, Mrs. Nathan Lifson and her daughter Matti.

Research Grants

continued

of an interleukin-5/diphtheria toxin conjugate protein and its cytotoxic activity against rat antibody-producing cells.

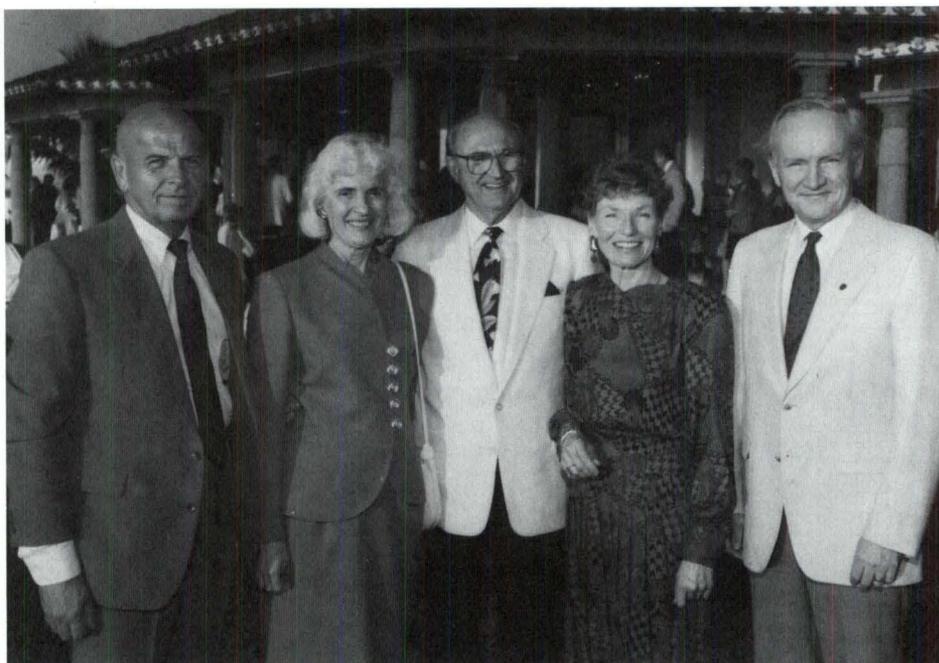
Special grants include: **Mark V. Dahl, M.D.**, Dermatology, \$10,000, Modulation of keratinocyte function; **Denise Goodman, M.D.**, Pediatrics, \$10,500, Regulation of cellular metabolism and function by adenylate kinase; **Robert A. Gross, M.D., Ph.D.**, Neurology, \$8,635, Calcium channel regulation by anticonvulsant drugs; **Bruce Eric Hammer, Ph.D.**, Radiology, \$10,000, Nuclear magnetic resonance imaging of flow and metabolites in hollow fiber bioreactors; **Emmanuel Katsanis, M.D.**, Pediatrics, \$11,000, Role of adhesion molecules in the immune response against neuroblastoma; **Gregory M. Vercellotti, M.D.**, Medicine, \$10,000, THERMOmax Kinetic Microplate Reader, Department of Medicine collaborative equipment grant proposal; and **James G. White, M.D.**, Laboratory Medicine & Pathology, Pediatrics, \$5,000, Improved detection of immunogold-silver staining of antigens on blood platelets. □

MMF names new staff member



Mark J. Marshall has been named director of alumni relations at the Minnesota Medical Foundation. He will be responsible for coordinating all events and programs of the University of Minnesota Medical Alumni Society, overseeing MMF's annual phonathon, and serving as the contact person for all alumni of the University of Minnesota Medical School.

Marshall was previously associate director of development at Marian Catholic High School in Chicago Heights, Illinois. He received his B.A. degree in history and political science from St. Olaf College in Northfield, Minnesota, where he was chair of the Senior Class Gift Committee and supervised the St. Olaf Parent and Alumni Phonathons. □



A University of Minnesota Presidents Club reception was held in Naples, Florida, in March at the home of Richard and Gwen Condon (center and second from right). More than 100 guests enjoyed the event, which included plaque presentations to several Presidents Club members by University President Nils Hasselmo (far right). At left is David Teslow, President and CEO of the Minnesota Medical Foundation, and Pat Hasselmo.

New members elected to AOA

Thirty-five students from the 1992 and 1993 Medical School graduating classes have recently been honored with initiation into Alpha Omega Alpha (AOA), a national medical honor society whose purpose is to promote scholarship, encourage high standards in character and conduct, and recognize high academic achievement.

Election to AOA is a distinction that accompanies physicians throughout their professional careers, and is limited to those individuals whose scholastic achievements (pre-clinical, clinical, and National Board scores) place them in the upper 25 percent of their class.

The Alpha chapter of AOA was established at the University of Minnesota in 1908, making it one of the oldest chapters in the country.

AOA sponsors a number of programs including a visiting professorship, student essay award, and student research fellowships. The Alpha chapter at the University of Minnesota also sponsors scholarships that are awarded through the Minnesota Medical Foundation to promising medical students in the first two years of medical school.

This year's initiates from the 1992 gradu-

ating class include: Deborah J. Anton, Bloomington; Lisa S. Poss Benson, Willmar; Anthony N. Brown, St. Paul; John J. Cierzan, Rochester; Deanna J. Diebold, Minneapolis; Kevin J. Donnelly, St. Paul; James M. Fink, St. Louis Park; Lorna J. Fredrikson, St. James; Jeffrey K. Gori, Eden Prairie; Alan R. Hauser, Sleepy Eye; Heather L. Hollender, St. Paul; Rosemary H. Kelly, Rochester; Cheryl M. Klenow, Duluth; Joia S. Mukherjee, Huntington, New York; Julie S. Waltz, Stockholm, South Dakota; Kari J. Wessman, Crookston; and John W. Zimny, St. Paul.

Initiates from the 1993 graduating class include: Nancy M. Benegas, Sioux City, Iowa; Kevin W. Bowers, Pierre, South Dakota; Rachel A. Bye, Minneapolis; Sheri L. DeMartelaere, Detroit Lakes; Martha J. Fanning, Rochester; Marvin K. Froberg, Danbury, Wisconsin; Ekaterina Litkevitsch, Minneapolis; Steven A. Moen, Minneapolis; Michael G. Neste, St. Cloud; Alexander D. Nicoloff, Minneapolis; Lesley B. Otto, Minneapolis; David H. Park, Urbandale, Iowa; Todd E. Simo, Stillwater; Gary V. Skrien, International Falls; Kendall J. Strand, Hudson, Wisconsin; Anil K. Tadavarthy, Eden Prairie; and Steven B. Thom, Fergus Falls. □

Students support AIDS research

Students from Hopkins West Junior High School recently held a fundraiser to support AIDS research at the University of Minnesota Medical School. They presented a check for \$170 to Robert Burgett, associate vice president for development at the Minnesota Medical Foundation, on May 14.

The check represents donations received when the members of Mrs. Feno Rainaldi's 9th grade homeroom class held a car wash as part of the school's community involvement activities. □



Hopkins West Junior High School students presented a check to MMF for AIDS research at the University of Minnesota Medical School.

UMD scholarships awarded

Three second-year medical students at the University of Minnesota, Duluth (UMD), School of Medicine have been named recipients of the Charles M. and Ruth H. Bagley Scholarship Award.

Stephanie Carlson of Cambridge, Julie Reddan of Bloomington, and Arne Vainio of Bear River were awarded the \$1,500 scholarships May 2 at the School of Medicine's Parents' Day luncheon. All three students earned the recognition as a result of basic skills and understanding demonstrated in their clinical training.

The scholarships were first awarded in 1981 in recognition of longtime Duluth surgeon Charles M. Bagley, and were renamed in 1989 to include his wife, Ruth. Dr. Bagley played an instrumental role in the founding of the School of Medicine in Duluth.

In addition, two first-year medical students at UMD have been named recipients of the first annual Duluth Clinic Regional Scholarship Award.

This scholarship is awarded to students who have spent a significant part of their childhood in a rural community in north-eastern Minnesota, upper Wisconsin, or western Michigan and who give every indication of returning to one of these regions to serve as rural family physicians.

Mark Versich of Hibbing and Kris Viren of Hastings, formerly of Grand Marais, were awarded the \$5,000 scholarships at the Parents' Day luncheon. □



Medical students share the excitement of Match Day.

Family practice top selection at Match Day

Family practice was the most popular residency choice at this year's Match Day, held March 18, accounting for 25.5 percent of the matches. Medicine was second with 21.4 percent. Fifty-seven percent of the students chose primary care fields (family practice, medicine, and pediatrics).

More than half the students, 55 percent, will be staying in Minnesota, and

32 percent will remain at the University. Eighty percent of the students received their first or second choice of residencies.

The National Residency Match Program matches medical students with the available resident positions in hospitals throughout the country. Students rank their choices of residencies, and the institutions, in turn, rank their preferences of candidates. The computer completes the match. □

ALUMNI UPDATE

Dear Colleagues,

Spring is a very busy time for the Medical Alumni Society, highlighted by the annual University of Minnesota Medical School Reunions. The classes of 1932, 1942, 1947, 1952, 1962, 1967, 1972, and 1982 returned to campus the first weekend in June, with class members thoroughly enjoying the many activities, the good fellowship, and the lovely Minnesota weather.

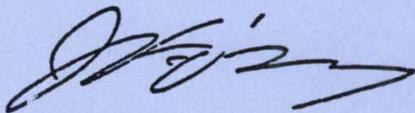
A very special event—for the fifth year in a row—was the Half Century Club Reunion, bringing together Medical School alumni from 1942 or earlier. A festive induction ceremony and luncheon honored the Class of 1942. Another extra special event this year was the 50-year reunion for University of Minnesota medical personnel who served their country in World War II as part of the 26th General Hospital Unit. It was wonderful to share the renewed friendships, the fascinating video show, and the memories with this very special group.

Recipients of the prestigious Harold S. Diehl Award, honored at the Medical Alumni Society Annual Meeting and Luncheon, are Frederic Kottke, M.D., '45, and William O'Brien, Jr., M.D., '46. Congratulations to these two fine representatives of the Medical School alumni. These honors are much deserved!

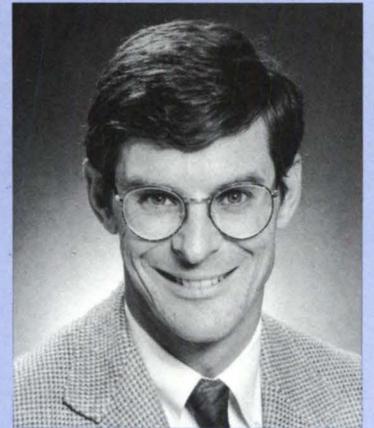
Annual winter receptions for friends and alumni of the University of Minnesota Medical School are in the planning process. California, outstate Minnesota, and other locations are possible sites for receptions. If you are interested in hosting a reception in your home, please contact the Medical Alumni Office. There will also be the annual University of Minnesota reception at the AAMC annual meeting in New Orleans this fall.

Comments, questions, or updates from alumni are encouraged and always welcome. Please don't hesitate to send them to the Medical Alumni Office, Minnesota Medical Foundation, Box 193 UMHC, Minneapolis, MN 55455, or call (612) 625-8676.

Sincerely,



John F. O'Leary, M.D. '77
President
Medical Alumni Society



Diehl Awards presented

Dr. Frederic J. Kottke, Class of 1945, and Dr. William A. O'Brien, Jr., Class of 1946, were selected to receive the 1992 Harold S. Diehl Award presented by the Medical Alumni Society at its annual luncheon meeting on June 6. Given in honor of the University of Minnesota Medical School's fifth dean, Dr. Harold Sheely Diehl, the award is presented to individuals who have made outstanding professional contributions to the school, the University, and the community.

Dr. Frederic J. Kottke

Dr. Kottke graduated from the University of Minnesota Medical School in 1945, specializing in physical medicine and rehabilitation. He became chairman and head of the Department of Physical Medicine and Rehabilitation at the University in 1952, and served in that capacity for 30 years. Throughout his career he was actively involved in the medical education of physicians and physical and occupational therapists, and trained many physicians who are currently the leading PM&R specialists in the country.

Dr. Kottke has made extensive contributions to the literature in his field, including basic and innovative concepts in rehabilitation medicine. His research continues to be highly respected and forms the basis for many therapeutic means followed today. He is senior editor of the basic handbook



Dr. William A. O'Brien, Jr. and Dr. Frederic J. Kottke, recipients of the 1992 Harold S. Diehl Award.

for PM&R which has been used for the past 25 years.

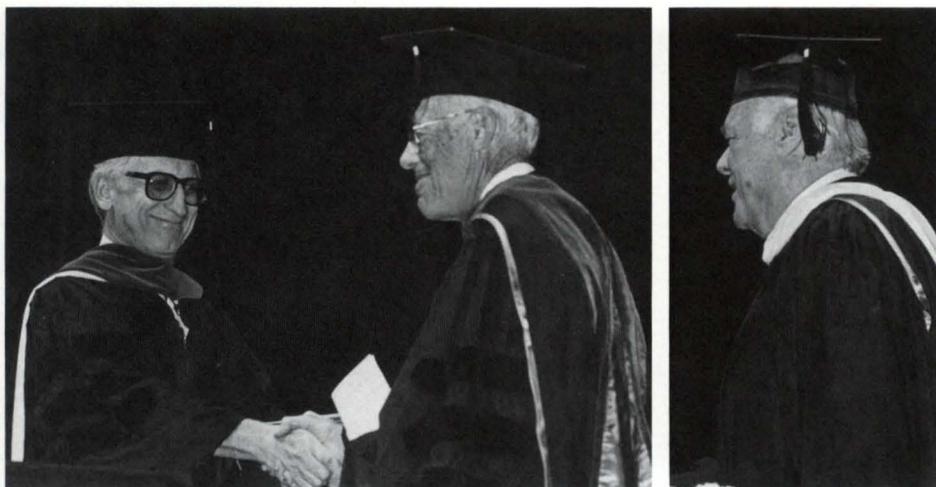
He has been chairman of the American Board of Physical Medicine and Rehabilitation, president of the American Congress of Rehabilitation Medicine, and president of the American Academy of Physical Medicine and Rehabilitation. He has also been involved with the community and has been very successful in bringing understanding of the needs for rehabilitation to lay people.

Dr. William A. O'Brien, Jr.

Dr. O'Brien graduated from the University of Minnesota Medical School in 1946. Since that time he has made numerous contributions in the fields of public health and preventive medicine and has had an active radio career, in addition to his extensive private practice in internal medicine and hematology/oncology.

Dr. O'Brien received a clinical instructor appointment at the University of Minnesota in 1956 in the Department of Hematology, and has since served as associate professor and professor. He has also served on the faculty of the School of Public Health, and has taught a University of Minnesota extension course in public health.

He began frequent community lecture-ships on understanding health and disease in the late 1950s, a practice which he has continued for more than 30 years. His first radio broadcast for WCCO Radio was in 1962, with topics covering a wide range of medical subjects. The preventive health message of Dr. O'Brien was received nationally during the 1970s through his syndicated radio program, "A Visit with the Doctor." He has been a frequent guest on other Minneapolis area radio stations, always presenting complicated medical topics in a language that listeners can understand.



Medical School professors Stuart Lane Arey and Malcolm McCannel received the University's Alumni Service Award from Vice President of Health Sciences Robert Anderson at the Medical School's commencement ceremony in June. Arey (center), a clinical professor emeritus of pediatrics, practiced family medicine and pediatrics in the Twin Cities for more than 40 years. McCannel, a clinical professor of ophthalmology, has practiced ophthalmology in Minneapolis since 1949 and is nationally recognized for his work in intraocular lens implantation and cataract surgery.

CELEBRATING REUNION

The first weekend in June brought more than 450 alumni and friends back to the University of Minnesota to celebrate their Medical School anniversaries. The classes of 1932, 1942, 1947, 1952, 1962, 1967, 1972, and 1982 gathered to reminisce, socialize, tour the Medical School, and find out what their classmates have been doing.

The Class of 1992 kicked off the activities with the First Reunion for the Class of 1992 on June 3. The event, sponsored by the Medical Alumni Society and the Minnesota Medical Foundation, provides graduating students the opportunity to reunite after two years of specialty rotations. Students and guests met at the Calhoun Beach Club in Minneapolis for one last gathering before graduation the

following Friday.

Campus and Medical School tours and a welcome reception were held on Thursday, June 4, for reunion attendees. Reunion headquarters were open throughout the day for early arrivals.

A very special event was also held this year on June 4—the 50th reunion of officers, nurses, and enlisted men who served their country and the University of Minnesota as members of the 26th General Hospital in World War II. Drs. Norman Holte and Russell Lindgren served as co-chairs of the event, which brought together more than 100 former members of the 26th unit.

The Half Century Club, formed in 1988 to bring together those who graduated 50 years ago or more, started the Friday morning activities with a presenta-

tion by Dr. John Wild. Dr. Wild recently received the Japan Prize for his pioneering work in ultrasound medical imaging. The Half Century Club Luncheon featured Medical School Dean David M. Brown, followed by an induction ceremony for new members of the Club.

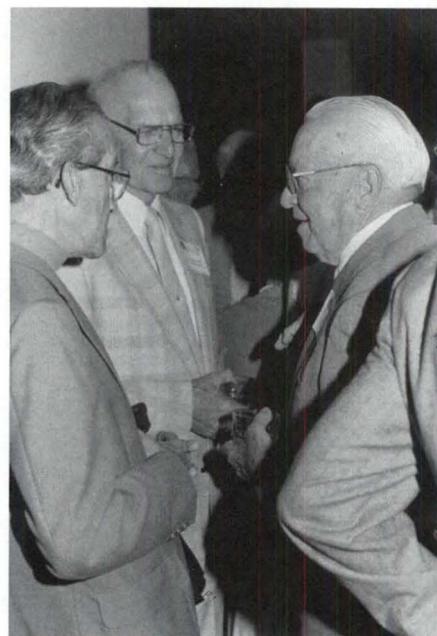
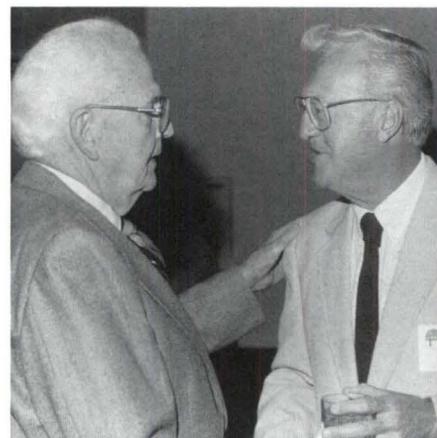
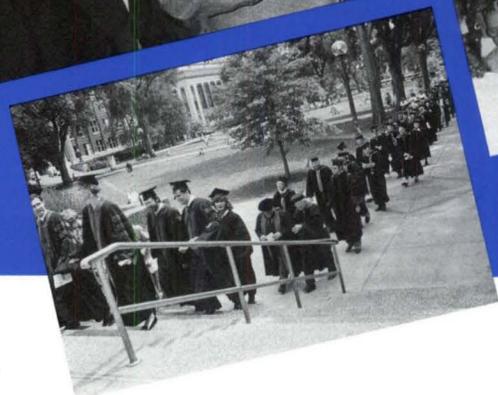
The Medical School Alumni Golf Tournament, held for the fifth year, was once again a much-enjoyed part of Reunion Weekend. Participants played a challenging round of golf at Les Bolstad University Golf Course.

This year's winners of the golf tournament were Dr. Robert Flaig, '62, from Walnut Creek, California, and Dr. James Testor, '52, from Winona, Minnesota.

The highlight of the Reunion Weekend was Friday evening's dinner and programs. All class members gathered for a



Half Century Club



WEEKEND

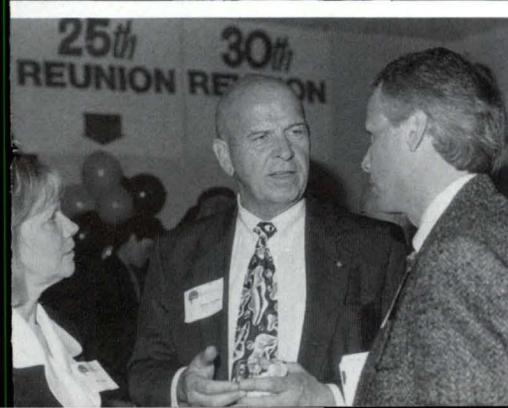
reception at the University Radisson Hotel, and later enjoyed dinner and special programs with their classmates.

Reunion Weekend concluded on Saturday with New Horizons in Minnesota Medicine and the Medical Alumni Society Annual Meeting and Luncheon. New Horizons is a continuing medical education program featuring faculty members of the University of Minnesota Medical Schools. Presentations were made this year by Drs. Dean Abrahamson, Richard DeWall, Elwin Fraley, Margaret Hostetter, June LaValeur, and James Priest.

The MAS Annual Meeting and Luncheon featured election of new board members and officers, and presentation of the Harold S. Diehl Award to Drs. Frederic J. Kottke and William A. O'Brien, Jr.



26th General Hospital



CLASS NOTES

1921

Dr. Harold C. Stratte, Windom, Minnesota, celebrated his 98th birthday in April and remains active traveling, writing, playing bridge, and exercising. He retired from his family practice only a few years ago, and advises others to keep busy, like your job, and enjoy your activities, friends, and family.

1942

Dr. Irving C. Bernstein, Minneapolis, was honored in April by the Minnesota Psychiatric Society as the Private Practitioner of the Year for 1991. The award recognizes clinical skills, teaching, scientific research, community involvement, and professional leadership. Dr. Bernstein served on the clinical faculty of the University of Minnesota for more than 30 years, teaching students and residents in psychiatry, obstetrics, and gynecology.

1945

Dr. Frederic J. Kottke, Minneapolis, has been elected a Distinguished Member of the Association by the Association of American Physiatrists. Requirements for this honor include international status and recognition by the membership as a major contributor to the field of physical medicine and rehabilitation (PM&R) in teaching, research, and scholarly publication. Dr. Kottke has been associated with the University of Minnesota since 1939 and was head of the Department of PM&R from 1952-1982. He is currently professor emeritus.

1956

Dr. H. Jerome Stulberg, Beverly Hills, California, radiologist for 30 years, was named Alumnus of the Year by Cedars Sinai Medical Center in Los Angeles. Dr. Stulberg is also clinical professor of radiology at Martin Luther King Hospital, Charles Drew Medical School, in Los Angeles.

1961

Dr. Karen Olness, Cleveland Heights, Ohio, was elected president of the National Society for Behavioral Pediatrics for 1991-92. She is also the principle

investigator on two NIH-funded grants to study AIDS in Ugandan children.

1975

Dr. Donald A. Baker, Spokane, Washington, has received his second patent award in the field of fetal health. NASA assisted Dr. Baker in developing a passive fetal heart sound transducer. His first patent, received three years ago, embodied a portable computerized passive non-stress testing unit.

1978

Dr. Joseph Gryskiewicz, Eden Prairie, Minnesota, was given the Humanitarian Award from the University of St. Thomas in March. He is a 1972 graduate of the school. The award is presented for outstanding contributions to the spiritual and material betterment of people who are less fortunate. Dr. Gryskiewicz is a plastic surgeon who volunteers time away from his Twin Cities practice to perform needed surgery on poor children in South America. He has treated several hundred patients during his four trips to Ecuador, and returns to the country for two weeks each year.

1981

Dr. Paul C. Matson, Mankato, Minnesota, has been inducted as a fellow into the American Academy of Orthopaedic Surgeons. The Academy is the largest medical association for musculoskeletal specialists.

1983

Drs. Leslie R. Buhr and Anna Marie B. Gonzalez, Kerman, California, are working in San Joaquin at a rural health clinic. Dr. Buhr also works part time in Clovis at a clinic serving Native Americans.

1985

Dr. Christina Pieper-Bigelow, Hastings, Minnesota, recently went into practice with the River Valley Clinic in gastroenterology. The clinic serves Hastings, Northfield, Farmington, Cannon Falls, Cottage Grove, Woodbury, and Forest Lake.

IN MEMORIAM

George S. Bergh, Sr., M.D.,

Class of 1932, retired Minneapolis surgeon and professor emeritus at the University of Minnesota Medical School, died April 17 at age 83. Dr. Bergh served in World War II in the U.S. Army as a member of the University of Minnesota 26th General Hospital unit based in North Africa and Italy. He received a Bronze Star for his work treating U.S. pilots. Dr. Bergh was on staff at Lutheran Deaconess Hospital in Minneapolis until his retirement in 1976, and was chairman of the board of the medical library at the VA Medical Center for 30 years. He is survived by his wife, Patricia, his sister Dr. Solveig Bergh, three children, and four grandchildren. Memorials are suggested to the Luthard N. Bergh Memorial Fund at the Minnesota Medical Foundation.

David L. Howard, M.D.,

Class of 1970, a family practice physician, died on February 15 in Superior, Wisconsin. He was 47. Dr. Howard is survived by two children, his mother, and a sister.

Heber S. Hudson, M.D.,

Class of 1950, psychiatrist from Albuquerque, New Mexico, died in March.

Charles W. Jarvis, M.D.,

Class of 1946, a pathologist at St. Paul Children's Hospital, died March 5 at age 71. Dr. Jarvis grew up in China as a child of medical missionaries, and currently was supporting the community development work of his daughter's family in Uganda. He was on staff at five Twin Cities area hospitals during his career, including Children's, Miller, Lakeview in Stillwater, and Riverview and Midway in St. Paul. He joined Children's in 1960, and was instrumental in establishing the hospital's pediatric lab and

pioneered many pediatric lab procedures. Dr. Jarvis also helped start the education program at Children's for medical students and residents. After he retired in 1986, Dr. Jarvis did pathology work for the University of Minnesota Raptor Center. He is survived by his wife, Dorothy, three children, and six grandchildren.

Paul H. Lober, M.D.,

Class of 1943, former chief of surgical pathology at the University of Minnesota Hospital and Clinic and professor of pathology at the University, died March 26 at age 72. Dr. Lober was chief of surgical pathology for more than 20 years, and taught at the University for 23 years. He was a surgical pathologist at Abbott Northwestern Hospital in Minneapolis in the 1970s and began a pathology residency program there. Dr. Lober was a fellow in the College of American Pathologists and a member of American Society of Clinical Pathologists, International Academy of Pathology, American Association of Pathologists, and a diplomate of the American Board of Pathology. He is survived by his son and his sister.

A.D. (Don) Mattson, M.D.,

Class of 1939, general practice physician, died February 27 at age 78. Dr. Mattson practiced medicine in St. James, Fairbault, and Willmar, Minnesota. He is survived by his wife, Ruth, three children, and seven grandchildren.

Marjorie Rowntree, M.D.,

Class of 1932, died recently in her hometown of Louisville, Kentucky.

Joseph O. Rude, M.D.,

Class of 1928, a Southeast Alaska resident since his graduation from Medical School, died in January at age 96. During his early years in Petersburg, Alaska, Dr.

Rude made house calls by boat and seaplane. The family later moved to Juneau, where he continued practicing for 48 years, including regular visits during his retirement to surrounding communities which were without doctors. Dr. Rude was active in numerous community activities, including the local school boards, the Boy Scout Council, and the Salvation Army board of directors. At the age of 90, he was featured in *USA Today* as a recreational skier at Juneau's Eaglecrest Ski Area. Dr. Rude is survived by four children, 11 grandchildren, and 10 great-grandchildren.

Arthur C. Skjold, M.D.,

Class of 1929, a surgeon in Minneapolis for more than 40 years, died March 28 at age 90. He had retired from practice in 1975. Dr. Skjold was a fellow of the American College of Surgeons and was head of the medical staff for the Zuhrah Shrine Circus for more than 20 years. He was active in the Shriner's chanter and jester units, and was a board member of the Minnesota Masonic Home. He is survived by his wife, Georgia, and four children.

Thorsten Smith, M.D.,

Class of 1933, of Edina, Minnesota, died in March at age 83. Dr. Smith was born in Fredrickstad, Norway. He received a post-graduate degree from Columbia University in psychiatry, and was a diplomate of the American Board of Psychology-Neurology and an American Psychiatric Association fellow. Dr. Smith is survived by his wife, Esther, three sons, and seven grandchildren.

John P. Storaasli, M.D.,

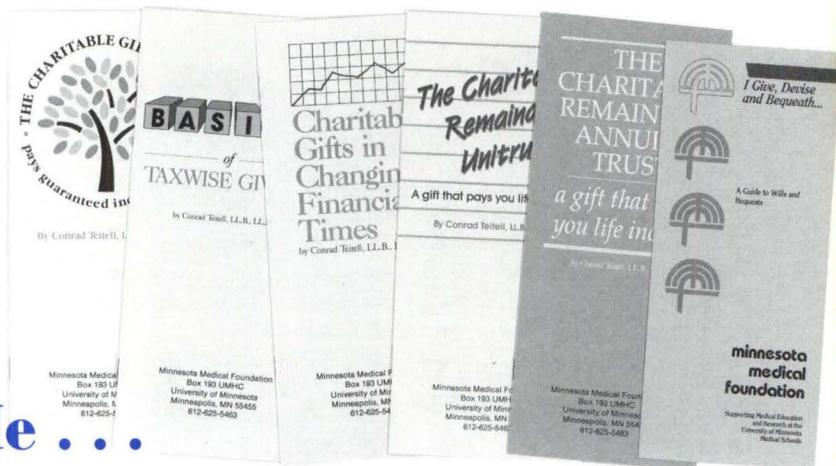
Class of 1945, died recently in Sarasota, Florida, at age 70. Dr. Storaasli taught and practiced radiology in Cleveland for 36 years, and helped pioneer therapeutic uses of radioisotopes to treat cancer and

hyperthyroidism. He was chairman of the Radiation Oncology Department at University Hospitals of Cleveland and professor of radiology at Case Western Reserve University. Dr. Storaasli served on the National Advisory Committee of the American Cancer Society and participated in the Atomic Energy Medical Research Project. He is survived by his wife, Iris, two children, and four grandchildren.

We have also received notice of the following:

Margaret Peterson,

Wife of University of Minnesota neuro-radiologist Harold O. Peterson, died March 6 at age 80. Mrs. Peterson had served as president of the Ramsey County Medical Society Auxiliary, the Minnesota Medical Association Auxiliary, and on the board of the University of Minnesota Hospital Auxiliary. She also organized the University of Minnesota Radiology Wives Group. Memorials to the Margaret F. and Harold O. Peterson Chair in Neurology at the Minnesota Medical Foundation were suggested. Mrs. Peterson is survived by her husband, Dr. Harold Peterson, and three sons.



Please Send Me . . .

If you're like most people, from time to time you receive letters offering information on some subject. It may or may not be what you need. In this issue of the *Medical Bulletin*, we would like to give you the choice of selecting from a number of publications we have available. If you don't see the information you would like, please let us know.

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SU92

THANKS FOR GIVING

Dr. Eva-Jane Ostergren Larson

by Jean Murray

Dr. Eva-Jane Larson may hold the record for the number of ties to the University of Minnesota Medical School. Her father, Dr. Edward Ostergren, graduated from the Medical School in 1909. Eva-Jane and her sister, Lenore, both followed in their father's footsteps and were Medical School graduates in 1938 and 1945, respectively. Lenore's husband, Kenneth Nimlos, was a 1945 Medical School graduate, and Eva-Jane's husband, Bert, bending tradition just slightly, was a 1937 graduate of the Dental School.

The next generation of Medical School graduates includes Bert and Eva-Jane's son, Bert (1972), daughter, Jane Reiman (1969), and son-in-law, Herbert Reiman (also 1969), as well as Kenneth and Lenore's two children, John (1972) and Robert Nimlos (1979).

And if that weren't enough, Dr. Larson's maternal grandfather, Olaf Swenson, was a contractor who built Millard Hall and the Anatomy Building at the University of Minnesota Medical School.

The ties to the Minnesota Medical Foundation are equally strong, where it is safe to say Dr. Larson holds another rather remarkable record. She has made a gift to MMF every year since its founding in 1939—53 years of generous support starting the year after she graduated from Medical School. She also served on the MMF board of trustees for eight years.

Dr. Larson was born in St. Paul and practiced there for 42 years, joining her father in his Payne Avenue family practice after completing her studies. Her son would later join the same practice for seven years, in the Medical Dental Build-



Dr. Eva-Jane Ostergren Larson

ing where her husband was a dentist.

Eva-Jane's father was a strong influence on her choice of medicine as a career ("He had me counting bones when I was 3.") and she loved biology in high school. Her most memorable class in Medical School was pathology with Dr. E.T. Bell, and she also remembers Dr. Andrew Rasmussen, teacher of neuroanatomy. "Who could forget his rapid-fire

presentation of a complicated subject and his chalkboard pictures of the pathways that didn't seem to make sense until the end of the course?"

A strong advocate of women in medicine and better living conditions for women medical students, Dr. Larson became very active in Alpha Epsilon Iota, the women's medical sorority. She served as executive secretary of the national chapter, and was involved locally in the successful effort by women students and alumni to raise money for purchase of a house near campus. She has continued to support AEI throughout her career.

Dr. Larson received the Harold S. Diehl Award in 1981, given for outstanding service to medicine and to the community by the Medical Alumni Society, and has also received the Woman of the Year Award from the Minnesota Women Physicians.

She currently lives in Rochester, close by the Mayo Clinic, and despite suffering from macular degeneration is able to give a great deal of care to her husband, who has Parkinson's disease. Her enthusiasm for life and learning has not diminished with the years, and she regularly attends symphonies and lectures in the area. She recently reflected with pleasure on a history of medicine lecture series she is currently attending ("from the Big Bang to the present"), and concluded, "I always thought heaven would be music and learning and friends . . . but I guess I have all that now."

Dr. Eva-Jane Ostergren Larson has enriched the lives of many people. We are deeply grateful for her generous tradition of giving and caring.





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Breezy Point Resort, Brainerd
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July 16-19

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September 12-13

Radiology '92: Imaging and Intervention

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