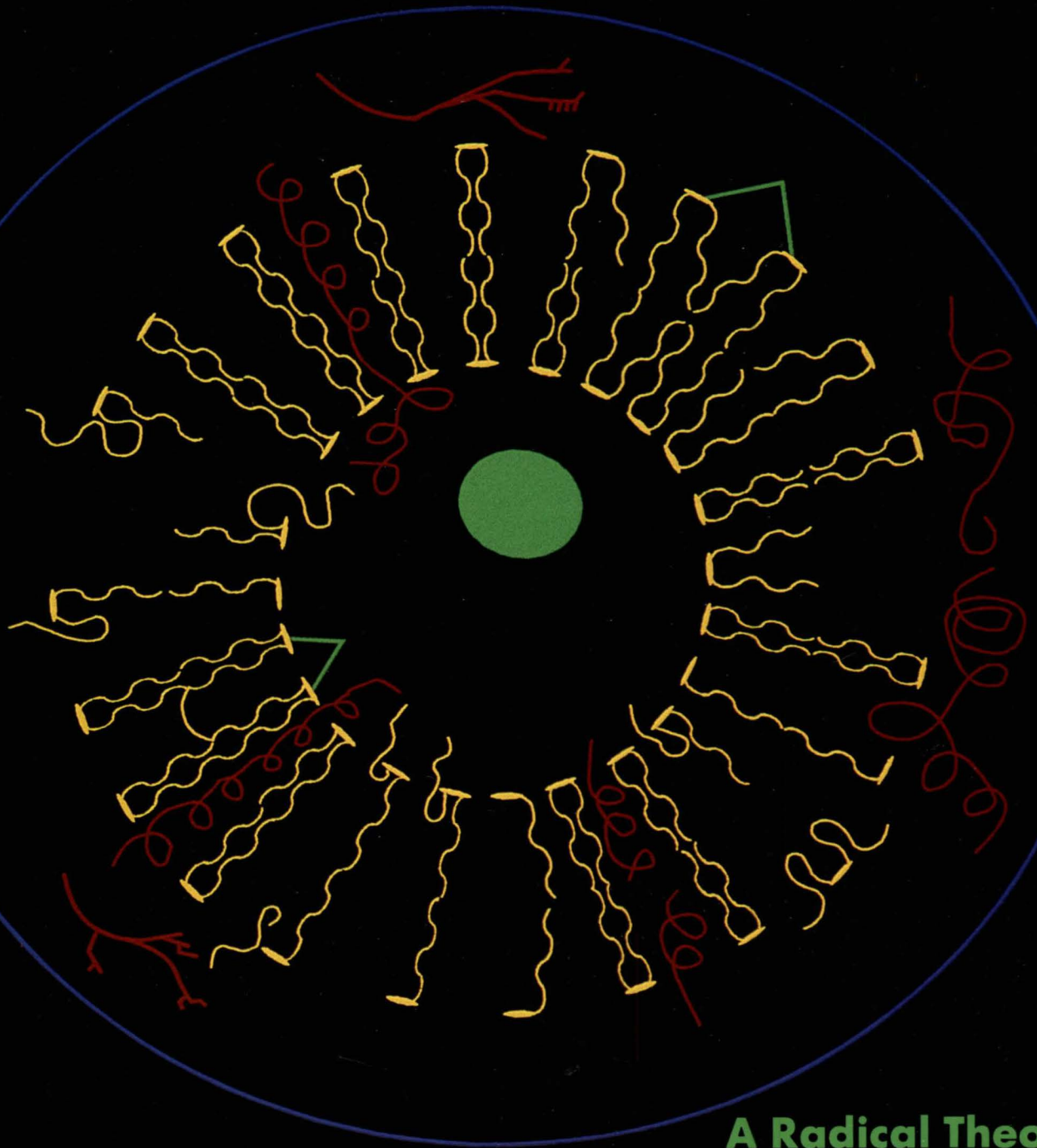


UNIVERSITY OF MINNESOTA

MEDICAL

BULLETIN

SUMMER 1988



**A Radical Theory
of Cell Damage**

A PUBLICATION OF THE MINNESOTA MEDICAL FOUNDATION

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Hunting the Dangerous Free Radicals **2**

Discoveries by basic researchers at the University of Minnesota are leading to attempts to reduce tissue damage and prevent many diseases.

Researchers of Merit **9**

Medical School investigators receive prestigious MERIT awards from the National Institutes of Health.

Practicing Real Medicine: The UMD Preceptorship Program **12**

Medical students learn firsthand the joys and frustrations of life as a family physician.

Medical School Graduation: A Centennial Celebration **16**

Students take the oath for new physicians at the 100th commencement ceremony in June.

Medical School Newsbriefs **18**

MMF Report **23**

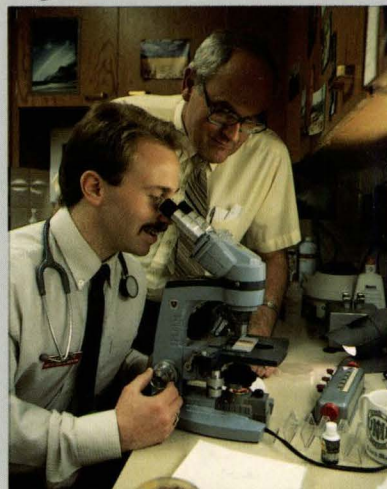
Alumni Update **26**

Historical Perspective **inside back cover**

Calendar of Events **back cover**



Page 2



Page 12



Page 16

The Minnesota Medical Foundation was founded in 1939 by a dedicated group of faculty members and medical alumni who saw the need for private support to build a strong future for the Medical School. A non-profit organization, MMF raises and disburses funds for medical education and research at the University of Minnesota Medical Schools in the Twin Cities and Duluth.

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On the Cover: Representation of an oxygen free radical attack on a cell membrane. Graphic courtesy of The Upjohn Company.

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The Wonders of Biological Growth Controls — Unlocking Mysteries through Basic and Clinical Sciences

Growth is important to all cells. Whereas, genetic predisposition is a major determinant, growth is influenced by stimulants and by the environment created by the cells themselves. Three important scientific discoveries occurred almost simultaneously: clinical scientists discovered growth hormone, the pituitary gland factor that regulates growth in children; basic scientists realized that nerve growth is regulated by a protein called nerve growth factor; and plant biologists discovered that plant growth is controlled by substances which behave similarly to animal cell growth factors. Then it was discovered that growth hormone itself is not directly responsible for its actions upon cartilage, but action is attributable to a liver protein called somatomedin.

It was inevitable that scientists would realize that the most potent growth hormone is insulin. Because somatomedin shares many of the effects of insulin, it was renamed insulin-like growth factor one. Another growth regulatory substance was named insulin-like growth factor two. It took molecular biologists to assure us that these insulin-like substances represent distinct proteins whose genes are under different regulation. It was only a matter of time before biologists discovered distinct growth factors derived from fibroblasts, skin epidermal cells, endothelial cells, and platelets which are important in wound healing.

The growth factor family has expanded further. Who could have imagined that in lower vertebrates a growth factor is derived from salivary glands? Why would growth be regulated by a gland that responds to the presence of food? Another growth factor called angiogenin regulates the growth of blood vessels into tumors. Some of the newest members of the growth factor family stimulate bone marrow cells which eventually become blood granulocytes and platelets. A recent article suggests that these proteins might be useful in decreasing the bone marrow depressant effects of the highly toxic agents used to treat cancer.

What should we make of the recent observations that growth factors have similarities to so-called oncogenes, DNA material with different expressions in tumor cells? Do tumor cells themselves have the potential to regulate growth?

Scientists and technicians are now delving into the mysteries of the regulation and mechanisms of action of these growth factors. Using the tools of molecular biology, they are dissecting which portions of their structure are responsible for specific biological actions. Growth hormone and insulin produced by these recombinant DNA techniques have become standard therapeutic products.

A second family of factors which regulates cell growth is the group of proteins which surround clumps of cells called matrix proteins. They are called collagen, proteoglycans, laminin, and fibronectin, each relating to the others by distinct chemical features to form a complex glue. The proportions and exact nature of each of these differs from one to another type of cell. Cancer cells produce different matrix components than do normal cells.

Matrix proteins also are important in influencing cell organization, that is, how cells line up in relation to their neighbors. They influence the alignment of one pole or side of a cell to another. The matrix is a form of communication of cells with each other and their environment. Closely linked members of the matrix family of chemicals are linked to the inside of a cell by traversing cell membranes and to convey messages to vital constituents within cells. This process may influence cell shape and cell movement.

The more we learn, the more we wonder. Fortunately, there are students and basic scientists seeking to explore the wonderment. They and their colleagues, the clinical scientists, join in the exploration and recognize potential applications of these discoveries for improving the lot of all living things. Can anyone hope to beat the challenge, the opportunity or the excitement of being a participant in this adventure?

David M. Brown, M.D., Dean
University of Minnesota Medical School

HUNTING

THE DANGEROUS

free radicals

Discoveries by basic researchers are leading to attempts to reduce tissue damage and prevent many diseases

By Michael Moore

We owe our existence to plants, which, billions of years ago, produced enough oxygen to allow animals to evolve. The increasingly oxygen-rich environment was like a biological lure, coaxing new species from the organic soup of bacteria and primitive plants. Eventually, the earth teemed with beings whose most critical need was oxygen.

Who would have thought that this life-giving oxygen might also present a threat to life? But now a rapidly growing field of basic biomedical research is proposing just that. In their search for basic mechanisms of disease, scientists are focusing on the toxic potential of certain types of oxygen molecules called free radicals. If ways can be found to detoxify these free radicals, it may be possible to prevent many types of disease from ever gaining a foothold in the human body. Clinical trials of one such detoxifying substance have already begun at a handful of medical centers, including the University of Minnesota Medical School.

Michael Moore is a science writer for the University of Minnesota Office of Health Sciences Public Relations.

The free radicals

To use oxygen, body cells must convert it to water and carbon dioxide in a process called aerobic respiration. During this biochemical chain reaction, oxygen free radical molecules are generated as intermediates. They are called free radicals because each has an odd number of outer orbit electrons, making it very unstable and highly reactive with other molecules. Each may exist for only a fraction of a second before a catalyst transforms it into another type of molecule. If this chain reaction gets out of control, oxygen free radicals can literally blow cells, tissue, and even DNA apart.

Inside the body, the free radical chain reaction has been compared to a nuclear energy generator, which must be carefully contained in order to be productive. In fact, the most devastating and indisputable injury caused by oxygen free radicals is the radiation injury resulting from a nuclear explosion.

At a 1987 international conference on oxygen radicals and human disease, researchers presented an astoundingly wide variety of human woes in which free radicals are thought to be involved. The list includes killers of millions, such as malaria, cancer, atherosclerosis, and emphysema. It includes autoimmune diseases such as diabetes and rheumatoid

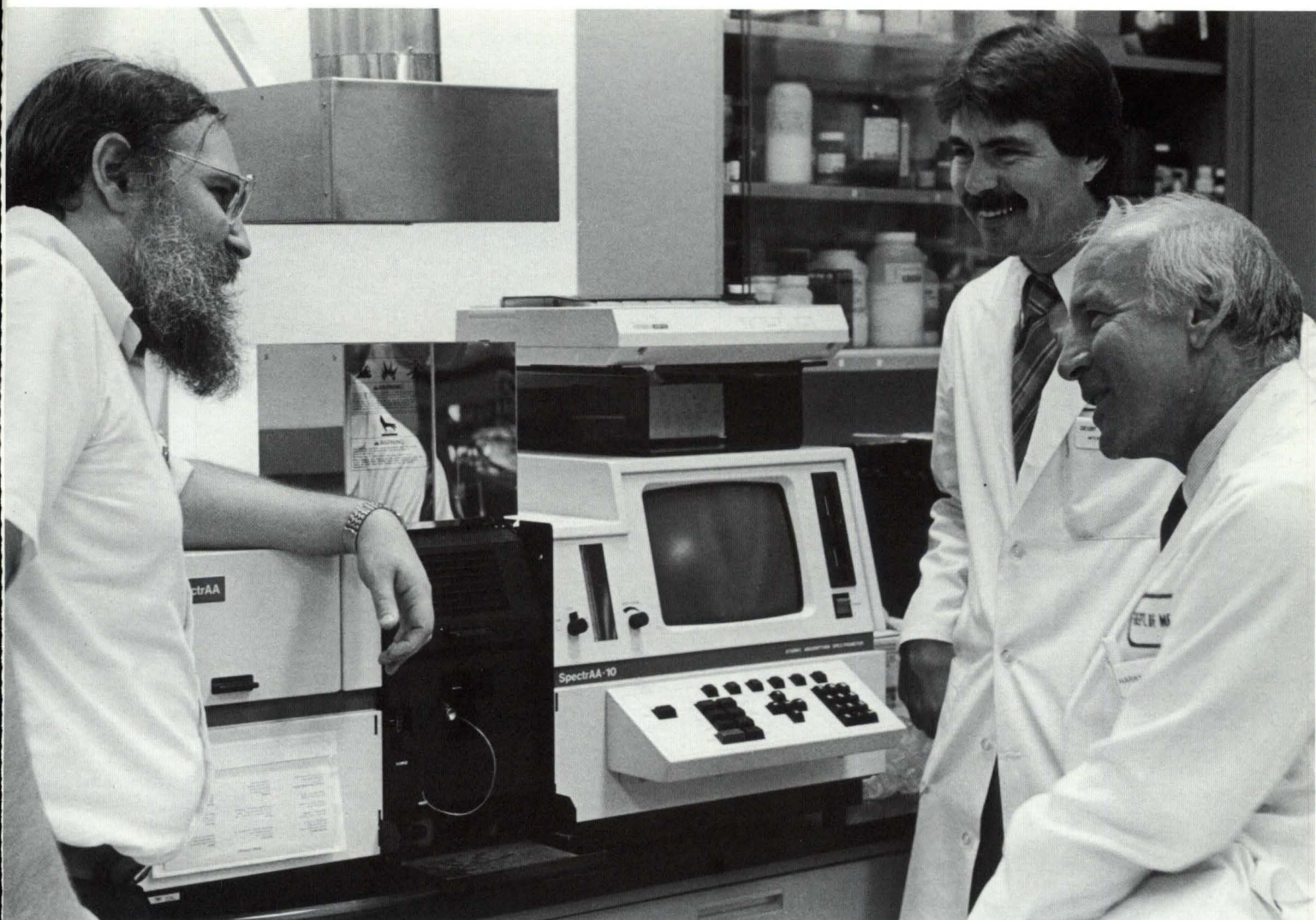
arthritis. Alcohol-induced organ damage, the effects of cigarette smoke, some brain disorders, and even the premature effects of aging are thought to be linked to oxygen free radicals. Clearly, finding a way to prevent such a basic cause of tissue damage would revolutionize medicine.

The scavengers

Understandably, aerobic organisms have had to evolve a host of natural defenses against injury from oxygen free radicals. Intracellular control is the front line of that defense. Oxygen is converted to water inside the controlled environment of the cell mitochondria to prevent oxygen radicals from reacting with cellular molecules.

And for each type of free radical molecule, there is a catalyzing enzyme that converts it to the next molecule in the reaction and one or more chemicals that act as scavengers of any uncontained free radicals. The discovery of one of these free radical scavengers by Duke University researchers Irwin Fridovich and Joseph McCord in the late 1960s set the stage for efforts to reduce free radical damage.

Fridovich and McCord found that superoxide anion, the molecule formed when one electron is added in the reduc-



Photos by Nancy Mellgren

tion of oxygen, is scavenged by an enzyme catalyst they called superoxide dismutase (SOD). McCord was able to isolate SOD in cells from every animal he studied, indicating its importance in the evolution of aerobic respiration.

The discovery of SOD led researchers to two other free radicals and their scavengers. The product of adding two electrons to molecular oxygen turned out to be hydrogen peroxide, which is scavenged by peroxidases. SOD speeds up the reaction in which superoxide anion becomes hydrogen peroxide. The most toxic free radical, hydroxyl radical, is formed by the reaction of hydrogen peroxide with iron ions.

The phagocytes

A second stage for studying free radicals was also set in the late 1960s. Dr. Paul Quie, now professor of pediatric infectious disease in the University of Minnesota Medical School, discovered a key clue to how the body defends itself against bacterial and fungal infections. Quie found that children with an

immune system disorder called chronic granulomatous disease had a defective ability to kill bacteria (or fungi) that were enveloped by white blood cells called granulocytes. Little was known at the time about this process, which is called phagocytosis. The fact that phagocytic killing could be defective suggested that the granulocytes must have specific mechanisms for killing microorganisms after enveloping them.

Quie's discovery launched intensive worldwide investigations of how granulocytes kill bacteria. The answer turned out to be another breakthrough in the understanding of oxygen free radicals.

After engulfing a microorganism, the granulocyte isolates it within a sac called a phagosome. The granulocyte then undergoes a respiratory burst during which it increases its oxygen consumption by as much as 20 times. This burst generates production of free radicals and bleach-like chemicals within containers called lysosomes. The granulocyte dumps the lysosomal contents into the phagosome, safely killing the captive microorganism.

Drs. Hammerschmidt, Vercellotti, and Jacob have extensive evidence that free radicals are the culprits in many disease conditions.

So not only has the human body developed a complex defense against free radical injury, it has also developed a potent offense using oxygen free radicals as toxins. Unfortunately, laboratory experiments suggest that sometimes our defense or offense goes awry and toxic oxygen is unleashed on body tissues. Several Medical School researchers are testing the hypothesis that free radicals may initiate some of the most devastating disorders affecting the human race.

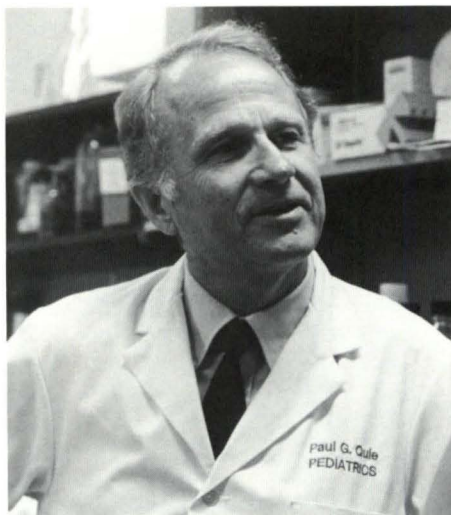
Frustrated phagocytes

Despite decades of research on atherosclerosis and heart disease, little is known about how the disease process starts. We know that a sticky substance called plaque builds up on injured areas of the endothelium (inner lining of blood vessels) and that saturated fats, cholesterol, and high blood pressure can influence the process. But what injures the endothelium in the first place?

Researchers in the Division of Medical Hematology have extensive evidence that free radicals are the culprits. In the late 1970s, division head Dr. Harry S. Jacob and Dr. Charles Moldow, now chief of medicine at the Minneapolis Veterans Administration Medical Center, pioneered studies showing that granulocytes stimulated by the body's immune system can injure the endothelium by exposing it to oxygen free radicals. Their research supported a theory of "frustrated phagocytosis," in which granulocytes try to envelope endothelial cells rather than microorganisms. Being much smaller than the endothelium, they cannot engulf it, and thus frustrated, they dump their toxic free radicals onto body tissue.

Jacob also performed pioneering research with former professor of surgery Dr. Richard Lillehei, showing that aspirin-like drugs could decrease damage to heart muscle by 30 percent following a heart attack. They theorized that by reducing inflammation, the drugs also decreased the number of granulocytes drawn to the damaged heart tissue, which resulted in less free radical damage.

Because of Jacob's preliminary findings, the Division of Medical Hematology has become a hotbed of research on tissue damage caused by free radicals. Early in the research the team investigated what stimulates the granulocytes to



Dr. Paul Quie discovered a key clue to how the body defends itself against bacterial and fungal infections.

be attracted to the endothelium and to attack it with free radicals. Jacob and Dr. Dale Hammerschmidt, associate professor of medical hematology, found that an immune system messenger known as complement may be involved. Complement is activated by the immune system to attract white blood cells to infected or damaged tissues.

Jacob and Hammerschmidt found that when activated complement was infused into the blood vessels of animals, it caused granulocytes to line the endothelium and stick together, sometimes becoming so dense as to disrupt blood flow to tissue in the area. After a few minutes the blood vessels began to leak, indicating that they had indeed been damaged by the granulocytes.

The researchers theorize that this type of blood vessel damage may be the cause of a devastating disorder known as adult respiratory distress syndrome (ARDS). It develops in some patients with extensive injuries or infections, and it can progress to failure of the liver and kidneys, often proving fatal. The hematologists' research shows that in ARDS patients with extensive bacterial infections the pulmonary blood vessels become damaged and leak plasma into lung tissue and alveoli, severely reducing the lungs' efficiency.

"There is a good deal of evidence that for most if not all ARDS patients the mechanism of damage is granulocytes margined along the pulmonary endothelium, damaging this tissue with oxygen radicals," Jacob says. "That has an intriguing paradox, because the method used to treat ARDS patients who have damaged alveoli and therefore can't oxy-

genate well is by having them breathe 100 percent oxygen at excess pressures. It is well known that if laboratory animals breathe 100 percent oxygen for four days they die of lung damage, which presumably is oxygen radical mediated. So in fact (in treating ARDS patients) you are feeding the fire while trying to keep the patient alive."

The hematology team found a cheap and very effective way to put out that fire, at least in laboratory animals. Dr. Gregory Vercellotti found that the lungs of rats can be protected from oxygen damage by infusing red blood cells into the alveoli during 100 percent oxygen therapy. The protective factor seems to be red cell glutathione, one of the most important cellular scavengers of oxygen free radicals.

The team also found another agent that proved to be protective in tissue culture models of ARDS and emphysema. Free methionine, a scavenger of free radicals formed in reactions with hydrogen peroxide, proved to have two beneficial effects that inhibited lung damage. First, it scavenged chloramine, a free radical known to inactivate alpha-1-antitrypsin, an enzyme that helps keep lung tissue flexible. And second, methionine prevented endothelial cells from detachment caused by granulocytes. This was the first indication that a free radical scavenger could play a dual protective role, preventing tissue damage and inactivation of an important enzyme.

The hematology researchers are now collaborating with colleagues in the Medical School to begin applying their research findings to help patients with ARDS. Jacob, together with Dr. Peter Bitterman, head of the division of pulmonary medicine, and Dr. Frank Cerra, professor of surgery, have applied to the National Institutes of Health to be a specialized center of research on ARDS and the related multiple organ failure syndrome.

A new risk factor

Despite all the intriguing laboratory evidence revealed by Jacob's team, it would be really exciting if evidence could be found for oxygen free radical damage in human populations. Unfortunately, free radicals are elusive characters. Because of their microsecond-long existence, they can only be detected in tissue cultures, not in living organisms, and only through

complex analysis involving chemoluminescence or electron spectrometry. Therefore, evidence for free radical damage results mostly from indirect tests performed on laboratory animals, usually by adding a known free radical scavenger to see if it prevents tissue damage thought to be caused by free radicals.

Human testing of preventive effects of free radical scavengers, or antioxidants, is just beginning, so it is too early to say if it will turn out to be therapeutic. But there is very strong — albeit indirect — evidence supporting the possibility that free radicals generated by granulocytes and other white blood cells play a major role in diseases of the circulatory system, and possibly cancer.

The evidence surfaced in epidemiological studies directed by Dr. Richard Grimm, assistant professor in the University of Minnesota School of Public Health. He reported in 1984 that in 6,400 men studied, those with the highest white blood cell (WBC) counts had an 80 percent greater risk of dying of a heart attack and a 40 percent greater risk of dying of cancer.

Grimm's findings prompted Hammerschmidt to survey the literature on the risk of ischemic (inadequate circulation of blood) diseases. He found that the WBC link has surfaced in almost every risk factor study, but the researchers simply didn't know what to make of it. "In retrospect, the fact that WBCs have been linked to damage to blood vessel walls and blockage of small blood vessels makes it perfectly understandable that a high count would be a major individual risk factor," Hammerschmidt says. He found that a high WBC count predicted a greater risk of heart attack and stroke both before and after an initial event.

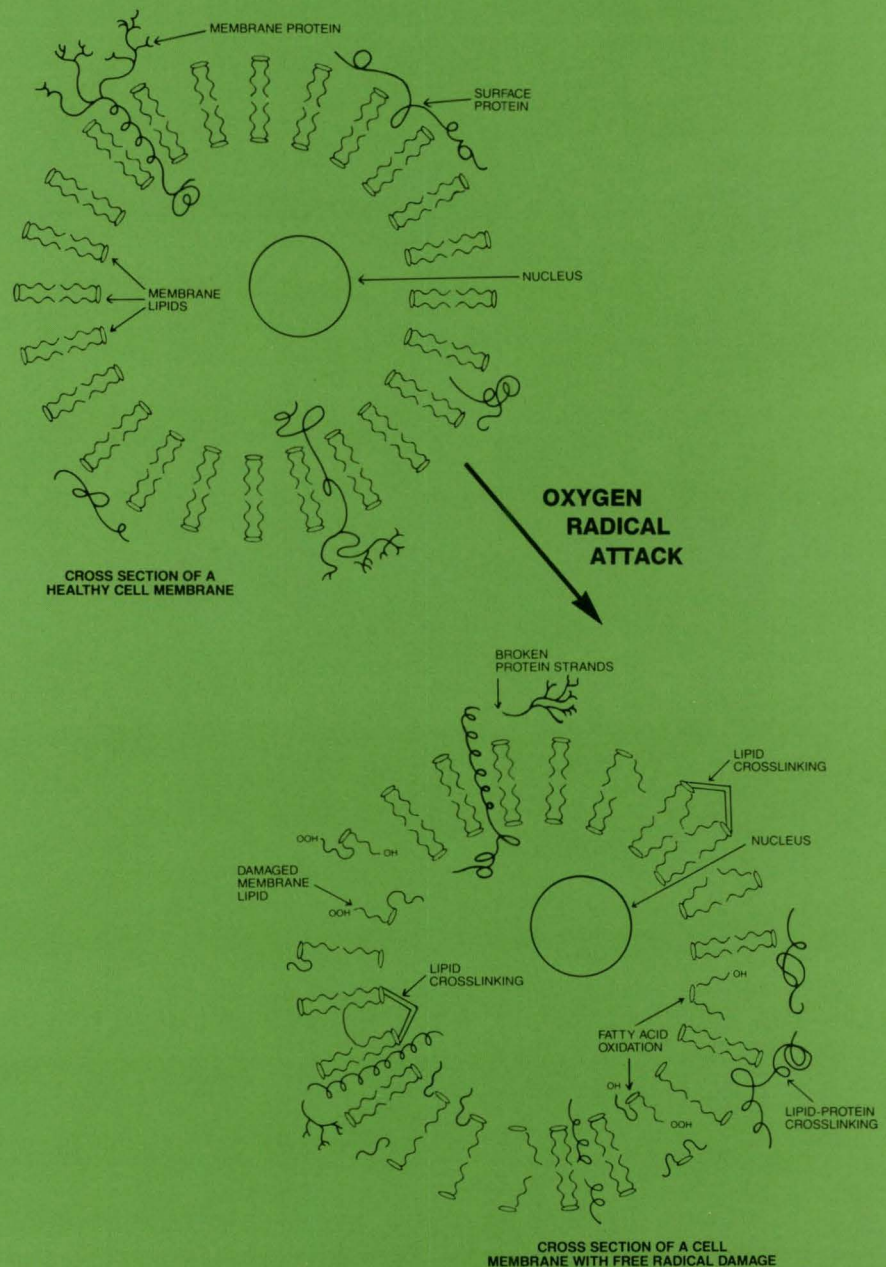
Because WBC counts can vary from day to day in individuals, Hammerschmidt points out that more sensitive tests of baseline WBC level and degree of granulocyte activation will be needed for a practical evaluation of individual risk of heart attack or stroke. But he says that he and other researchers feel that current WBC counts are the best predictors of ischemic events in an individual, especially when weighed along with the person's general risk factors, such as age, race, sex, smoking, blood pressure, and blood lipids.

How Oxygen Radicals Cause Tissue Injury

Oxygen Free Radical Attack on Cell Membrane

Sources of excess oxygen radicals include:

- tobacco smoke
- air pollution
- inflammation (from injury, trauma, rheumatoid arthritis)
- cured, dehydrated and stored meat
- animal/vegetable fats used in industrial frying



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Some Conditions Linked to Oxygen Radicals

Conditions	Number of New Cases In the United States per Year
CARDIOVASCULAR DISEASES	63,400,000*
RHEUMATOID ARTHRITIS	2,100,000**
CENTRAL NERVOUS SYSTEM:	
HEAD TRAUMA	450,000
SPINAL CORD INJURY	10,000
STROKE	500,000
EMPHYSEMA	191,000
CANCER	930,000
ADULT RESPIRATORY DISTRESS SYNDROME	150,000
MAJOR ORGAN TRANSPLANTS (does not include tissue transplants)	38,541
INFLAMMATION	—
AGING	—

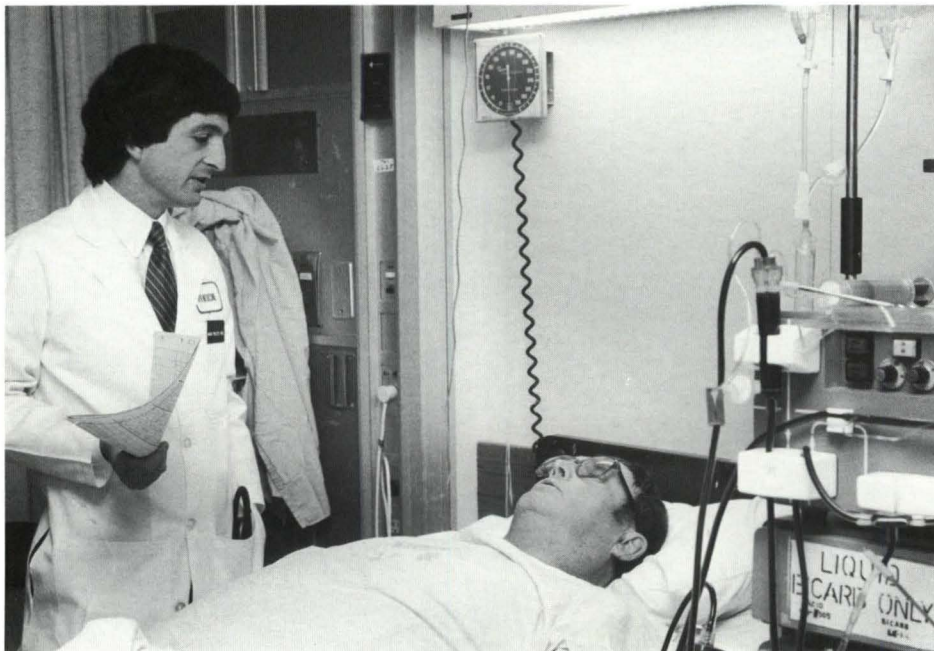
*Estimated total number of people with cardiovascular diseases as of 1984.

**Estimated total number of people with rheumatoid arthritis as of 1986.

From basic to bedside

The primary goal in treating ischemic events such as heart attack, stroke, or interruption of blood flow to any organ, is to restore the blood flow as quickly as possible. This prevents some of the damage to oxygen-deprived organ tissue. But paradoxically, an additional wave of tissue injury occurs when blood flow and oxygen are restored. This so-called reperfusion injury is thought to be caused by oxygen free radicals, because it can be prevented in laboratory animals by infusing a scavenger enzyme before restoring blood flow.

Clinical studies aimed at preventing reperfusion injury are now underway, thanks to almost 20 years of basic research that resulted in the discovery and testing of superoxide dismutase (SOD). SOD has now been bioengi-



Dr. Mark Paller talks with patient Roger Anderson, who had just recently received a cadaver kidney.

neered through gene-splicing technology and is therefore available as an experimental drug.

One of three clinical tests of SOD underway in the United States is being conducted at the Medical School by Dr. Mark S. Paller, an associate professor of medicine. Paller, a nephrologist, has been studying the effect of SOD in preventing

kidney reperfusion damage since 1982. He found a clear protective effect in kidneys of rats and dogs, and researchers elsewhere found the same in pigs.

Last fall, Paller and his colleagues from the Department of Surgery (Drs. Dunn, Fryd, Gruber, Matas, Najarian, Payne, and Sutherland) began enrolling patients in a clinical study of SOD in kidney

transplant recipients who receive a cadaver kidney. "We chose cadaver kidneys because the kidney has been taken away from its blood supply and has sustained an ischemic insult," Paller says. "Then when it's transplanted into the recipient it is well perfused. We know exactly when that happens, when the surgeons take the clamp off the renal artery after they've sewn the kidney into the patient. And in fact 30 to 40 percent of patients who get cadaver kidneys sustain some acute renal injury. We don't know how much of that injury is due to oxygen radicals and how much is due to other mechanisms."

Paller hopes the SOD trial will result in a clinically useful drug for transplant patients, and shed some light on the involvement of free radicals in reperfusion injury. He hopes to conclude the double-blind, randomized, placebo-controlled study by the end of the year.

Paller's results should become available at about the same time as the results of a multicenter trial elsewhere of SOD in heart attack patients, and another in patients with severe brain injury. These trials are drawing a great deal of interest from pharmaceutical companies and from Wall Street, because SOD is likely to be the next bioengineered drug to receive FDA approval, and because it is the first free radical scavenger to be tested in humans.

Toxic iron

Recently, Medical School researchers analyzing laboratory situations in which free radicals cause the most damage have begun pointing their fingers at a co-conspirator: iron. When hydrogen peroxide is present, iron catalyzes the formation of the hydroxyl radical, which researchers feel is the most harmful of the oxygen free radicals. It is thought to be especially active in breaking down, or peroxidizing, lipids, which are fat-soluble compounds that are important constituents in cells.

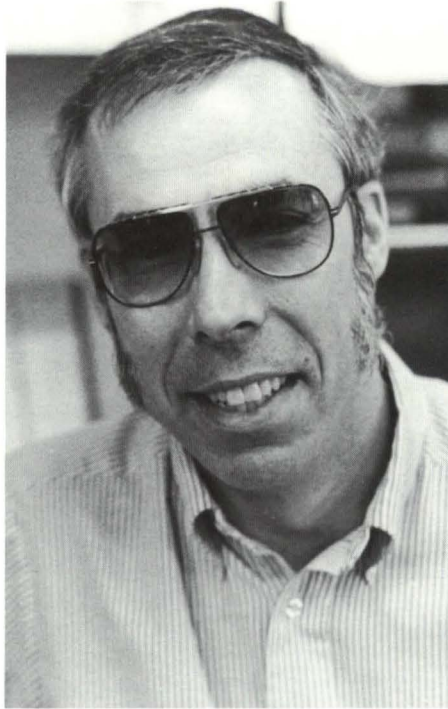
Measurements of lipid peroxidation are one of the indirect methods of detecting free radical activity. "When lipids are attacked by free radicals they can continue a chain reaction to destroy additional important cellular constituents such as other lipids, enzymes, and

nucleic acids," Paller says.

In his rat studies, Paller found that a compound called deferoxamine prevents kidney injury caused by the reaction of free radicals and iron. Deferoxamine is one of a class of compounds known as iron chelators, which detoxify iron and prevent it from reacting to form hydroxyl radical.

Vercellotti found that this same iron chelator protected the hearts of dogs after blood flow had been shut off and then resumed after 45 minutes. This could be of great clinical significance in preventing reperfusion injury to the heart after coronary bypass surgery or heart transplantation.

Iron chelators have caused an especially interesting turn in the research of Dr. John W. Eaton, professor of laboratory medicine and pathology. A geneticist, Eaton's laboratory research has taken him from the most basic studies of phagocytosis and DNA, to clinical studies of diseases such as malaria, to epide-



Dr. John Eaton has been instrumental in bringing together a number of researchers who are studying free radicals to exchange ideas.

miological studies of dietary fiber. He has been instrumental in bringing together researchers who are interested in free radicals who need a friendly but critical forum to try out some of their ideas and data. They gather together whenever Eaton's humorous prodding can stimulate enough interest for a meeting of what they've dubbed the Near East Radical Organization.

"This is an area in which the more you work on it the less you know," Eaton says wryly. "The people working on activated oxygen are beginning to realize that we don't understand the most simple, fundamental reactions, things that you always thought people knew, like how rust forms and why it doesn't form, how things become oxidized. There's a lot we don't know."

But a lot more is known now than before scientists became interested in free radicals, and Eaton has been in the thick of the discovery process. Much of his interest has been directed at the involve-

So that's why those drugs work!

The relatively new field of oxygen free radicals has given Dr. David Zoschke, a rheumatologist who is an assistant professor of medicine, some insight into existing therapies for rheumatoid arthritis. That insight has pointed him toward innovative strategies for improving treatment of the disorder.

Rheumatoid arthritis is initially treated with aspirin compounds, which reduce inflammation but don't affect the actual disease. If the disease persists, second-line agents such as gold injections, d-penicillamine, immuran, or methyltrexate are used. Zoschke explains that all these drugs were discovered useful in rheumatoid arthritis somewhat fortuitously.

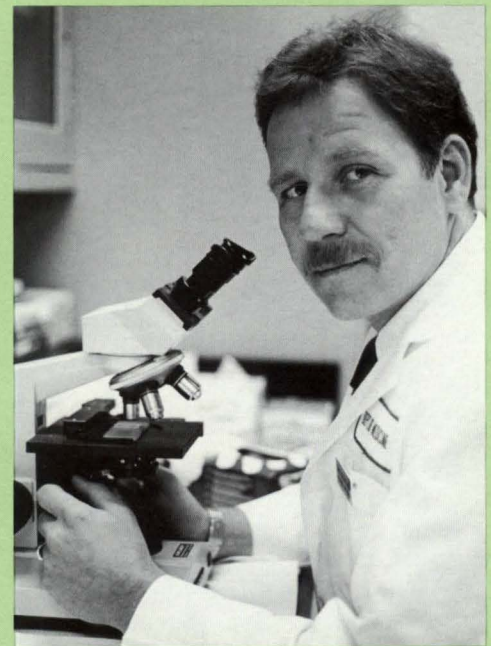
"Syphilis used to be treated with gold compounds, and they found that people with rheumatoid arthritis got better. D-penicillamine was used to bind up iron in certain iron overload states such as hemochromatosis. People with this also get rheumatoid arthritis and the treatment would help that. Nobody knows how these drugs work in rheumatoid arthritis, so we decided to see if they have any anti-

oxidant activity."

So far, Zoschke has found that d-penicillamine and immuran are both potent scavengers of hydrogen peroxide, but methyltrexate is not. And aspirin compounds may help by reducing inflammation and the resulting autoimmune attack that damages cartilage in rheumatoid arthritis. He is now testing new compounds that have a sulfhydryl group in their chemical makeup that seems to be the common thread in the drugs that are useful in scavenging free radicals.

Zoschke can test those new substances in a rabbit model of rheumatoid arthritis. This model has been instrumental in studying the possible role of free radicals as an initiator of rheumatoid arthritis. He has found that the immune system within a joint can be disregulated by free radicals, resulting in excessive white blood cell activity in the diseased part of the joint. This activity generates more free radicals, which aggravate the disease.

Zoschke is searching for effective ways of increasing free radical scavenging inside the joint, hoping to



Dr. David Zoschke is studying innovative strategies for improving treatment of rheumatoid arthritis.

improve on old treatments that are only now beginning to be understood.

How old is old?

In the Hunza valley of northern Pakistan, Dr. M. John Murray, professor of medicine in cardiology, had a rare opportunity to meet a people who have redefined the meaning of old age. Many of the Hunza live to be 100 years or older, and they remain quite vigorous to the end.

Murray and his wife, Anne B. Murray, a dietitian, observed the lifestyle of the Hunza centenarians and drew blood from five of them for analysis back at the University of Minnesota. They found that the Hunza diet is rich in antioxidants, or scavengers of free radicals known to damage body tissue. When the Murrays compared antioxidant activity of the blood of

the Hunza centenarians to control groups, they found significant reduction of lipid peroxidation, a marker of free radical damage, in the blood from the old people.

The Hunza get their antioxidant from the foods naturally available to them, especially from fresh vegetables, which are a rich source of carotene, vitamin E, and from apricots, which are a source of cyanide, a free radical scavenger that is poisonous in large amounts. Both carotene and vitamin E have been associated with low rates of cancer, and, if they are the key to the long-lived Hunza, they may contribute to a long life as well.

ment of iron in free radical damage, especially to DNA and as a possible cause of cancer.

"If you take clean DNA and add (the free radical) hydrogen peroxide to it, almost nothing happens and the DNA stays in one piece," Eaton says. "If you do the same experiment except contaminate the DNA with iron, the DNA is blown to smithereens. It's an absolutely stunning relationship. So there is clearly an iron-dependent reaction that causes the DNA to be damaged."

Eaton admits that the missing element in this stunning relationship is a mechanism to let iron into the cell nucleus, where it could affect DNA. But he has just begun studies of cigarette tar, looking for possible initiators of lung cancer. "We've found a substance in cigarette tar that has the ability to go down into a water phase, bind iron, and pull it into an organic phase. What this means in a biologic system is that this iron-binding system could go down into the water phase of the cell, it could bind iron, and then it could move into the nucleus. So it may be one of the missing elements we're looking for."

Eaton's laboratory evidence of the protective powers of iron chelators led him and a former research fellow, Dr. Ernst Graf, now with the Pillsbury Company, to study an iron chelator, phytate, which is present in cereal foods. In laboratory experiments, Eaton and Graf showed that

phytate binds iron very tightly and thereby prevents the generation of hydroxyl radical and the lipid peroxidation it normally causes.

Epidemiological studies show that a high intake of dietary fiber is associated with a low incidence of colon cancer. Using their new knowledge of iron chelation and free radicals, Eaton and Graf reexamined a hypothesis suggested in 1971 by D.P. Burkitt. He thought that it was the fiber content of the diet that protected against colon cancer.

Graf and Eaton's retrospective analysis of epidemiological studies of colon cancer suggested an alternative possibility. For example, a study of colorectal cancer in Denmark and in Finland found that the Danish people have a much higher incidence than the Finnish, even though the Danes consume almost twice as much dietary fiber as the Finns. When Eaton and Graf analyzed the phytate content of the two populations' diets, they found that the Finnish people eat more cereal foods and have a phytate intake 20 to 40 percent higher than the Danish people.

Eaton and Graf speculate that because phytate is mostly undigested it is available to block free radical damage in the colon caused by bacteria or minor inflammation. They pointed out that the noted association between colon cancer and high-meat, high-fat diets may be caused by the fact that these foods are rich in iron, which increases the toxicity

of free radicals.

Eaton's laboratory recently was successful in improving the biological usefulness of an iron chelator. The naturally occurring iron chelators are small molecules that don't survive long in the circulation. A former research associate of Eaton's, Phillip Halloway, "developed a way of taking a very powerful iron chelator and putting it on a large carbohydrate backbone," Eaton says. "One of the carbohydrates we used is dextran, which is used in medicine as a plasma substitute. So we can make very high affinity iron chelators that can survive a long time in the circulation."

Realizing the potential usefulness of the durable iron chelator, Halloway and several colleagues patented the product and applied for a small business grant. This enabled him to set up a small company, with the University as a part owner and profit sharer. The company is now working to develop the product as a drug.

Despite this foray into the "real world," Eaton remains mostly interested in the basic biology of oxygen free radicals. He recently received NIH grants to study microorganisms that cause devastating diseases such as leprosy, tuberculosis, and leishmaniasis. "These organisms have the capacity to live and reproduce inside phagocytes, and that's actually what makes them so dangerous, because they can survive inside the phagocyte despite being bombarded with lots of activated oxygen (free radicals)," he says. "So I'd like to know what kind of oxidant defense permits their survival."

If Eaton can find out how these bacteria survive despite constant toxicity inside the phagocyte, it may provide clues to how humans could prevent tissue damage from oxygen free radicals. The project is like a microcosm of the entire field of free radical research, which continues to look at very basic biological processes at the same time clinical studies are testing antioxidant treatments that have been found safe and effective in animal tests.

"I've got a theory about medical research," Eaton says, "that the more applied whatever you're doing is, the less likely it is to be a lasting contribution. I think the work that really lasts is the fundamental, really basic stuff. Don't you?"



RESEARCHERS OF *Merit*

Five Minnesota investigators receive prestigious NIH MERIT awards

By Elaine Cunningham

Beginning in July 1986, the National Institutes of Health (NIH) began offering a limited number of MERIT awards to investigators who had demonstrated superior competence and outstanding productivity during their previous research endeavors.

The purpose of these awards is to provide long-term stable support to those whose research performances have been distinctly superior. Long-term support fosters continued creativity and spares these researchers the administrative burdens associated with preparation and submission of research grant applications.

Five investigators at the University of Minnesota Medical School have been honored for their research achievements with the prestigious MERIT award. They are: Khalil Ahmed, Ph.D., professor of laboratory medicine and pathology at the Veterans Administration Medical Center; Robert J. Bache, M.D., professor of medicine; Harry S. Jacob, M.D., professor of medicine and of laboratory medicine and pathology; Horace H. Loh, Ph.D., professor and head of the Department of Pharmacology; and James G. White, M.D., regents' professor of pediatrics and laboratory medicine and pathology.

Investigators do not apply for MERIT (Method to Extend Research in Time) awards. After submitting research proposals in accordance with conventional NIH procedures, candidates are singled out for MERIT award consideration by NIH staff or members of the National Advisory Council.

Criteria for selection include: a regular research project grant application that is



Khalil Ahmed, Ph.D.

deemed highly meritorious by the initial review group; a past record of scientific achievement and demonstrated leadership in the research area addressed by the grant application; and an area of research of recognized importance or of special promise.

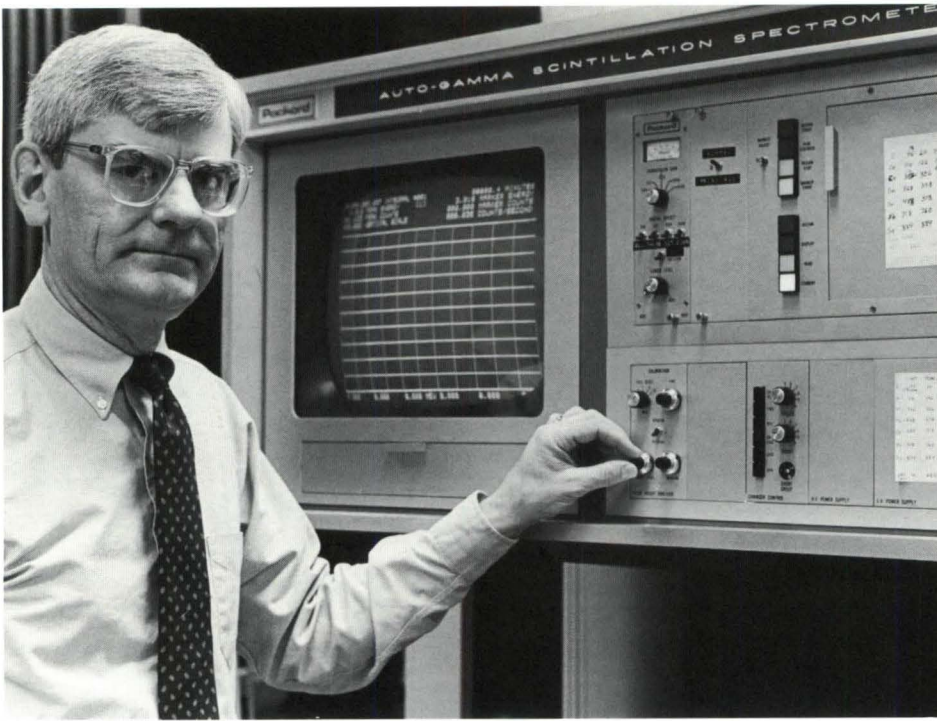
MERIT awards are granted for an initial period of three to five years. Based on a review of accomplishment, the award may be extended for an additional three to five years.

"We are extremely pleased that five of our Medical School faculty have been recipients of MERIT awards," says David M. Brown, M.D., dean of the University of Minnesota Medical School. "We are proud of their exceptional accomplishments and the recognition they have received for their research."

Khalil Ahmed, Ph.D.

Dr. Ahmed has been conducting research in the field of biochemistry for nearly 30 years. His special interests lie in biochemistry and functions of tissue phosphoproteins and the biochemistry of membrane transport function. His research efforts have been recognized with numerous grants from NIH, the Veterans Administration Central Office, the Minnesota Medical Foundation, the Minnesota Heart Association, and the American Cancer Society, among others.

His research project pertaining to the current award looks at the role of androgens in human prostate neoplasia. The long-term objectives of this research are to investigate the biochemistry of nuclear phosphoproteins and protein kinase



Robert J. Bache, M.D.

(PKs) with the aim of defining their role in the androgen-mediated gene action in rat ventral prostate, and to examine these parameters in human normal and neoplastic prostate to uncover any underlying alterations associated with such pathology. Ahmed has been collaborating in this research for nearly 10 years with Dr. Said Goueli, a research chemist and assistant professor in the Department of Laboratory Medicine and Pathology at the Veterans Administration Medical Center.

A native of Pakistan, Ahmed came to Canada in 1957 as a research fellow at McGill University in Montreal. He had received a B.Sc. and an M.Sc., both with honors, from Panjab University's Institute of Chemistry and completed his Ph.D. in biochemistry at McGill in 1960. He did post-doctoral study at the Wistar Institute at the University of Pennsylvania.

Before coming to Minnesota in 1972, he held positions as an assistant professor in the division of metabolic research at the Chicago Medical School, and as a senior staff research biochemist in the laboratory of pharmacology at the National Institutes of Health. He came to the University of Minnesota as an associate professor of laboratory medicine and pathology and was elevated to full professor in 1977. Currently, he is a research biochemist, a research career scientist, and chief of the cell and molecular biochemistry laboratory at the Veterans Administration Medical Center.

Robert J. Bache, M.D.

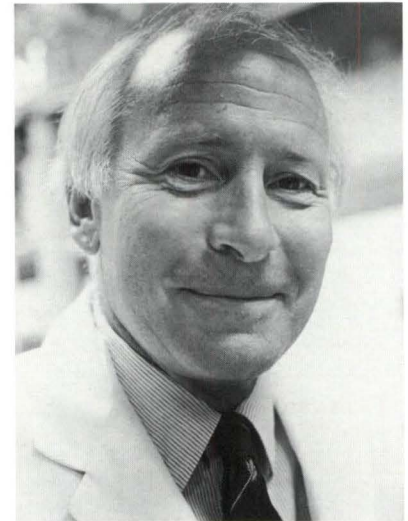
Dr. Bache has received three major research grants from the National Institutes of Health for projects involving coronary vascular function.

His current research, which was extended through the MERIT award, is entitled "The Coronary Vascular Response to Ischemia." His studies examine vasomotor characteristics of the coronary resistance vessels, both during unimpeded arterial inflow and in the presence of a flow-limiting stenosis. He also is examining the collateral channels which supply myocardium distal to an occluded coronary artery.

During the course of his investigation, Bache will try to answer questions such as: Does cold exposure cause coronary vasoconstriction which opposes metabolic vasodilation produced by exercise? Are the coronary collateral vessels capable of active vasoconstriction which may impair blood flow? Is the variability of this vessel development in response to coronary artery occlusion related to differences in the degree of native coronary collateral vascularity? Does chronic coronary artery occlusion cause an increase in the width of the perfusion boundary between adjacent normally perfused and collateral-dependent myocardial areas?

A major part of Bache's career has been spent at the University of Minnesota. After receiving his medical degree from Harvard University in 1964, Bache came to Minnesota to serve both his

internship and residency. He went on to serve a fellowship in cardiology at Duke University Medical Center, but returned to Minnesota in 1969 for further cardiology fellowship training and was appointed instructor of medicine the following year. In 1971, he was named assistant professor of medicine at Duke University, while concurrently serving as clinical investigator at the Veterans Administration Hospital in Durham, North Carolina. He was appointed associate professor at Duke in 1975. He came back to Minnesota in 1976 as an associate professor of medicine and was elevated to full professor in 1979. During his tenure at Minnesota, Bache received a Research Career Development Award from the United States Public Health Service.



Harry S. Jacob, M.D.

Harry S. Jacob, M.D.

Dr. Jacob received his MERIT award for his research into abnormal blood cell membranes in disease. His laboratory has been interested in the interaction of inflammatory cells with endothelial lining cells of blood vessels, and has demonstrated that granulocytes — normally beneficial cells by virtue of their ability to phagocytize and kill bacteria — can damage endothelial cells to which they become closely attached in diverse disease processes. This attachment and damage has been shown to be critically important in causing the acute lung injury, termed the Adult Respiratory Distress Syndrome, that frequently occurs after trauma or severe infection.

In addition, this inflammatory cell/

endothelial cell interaction may be importantly involved in the vascular damage underlying atherosclerosis. Jacob's laboratory has pioneered in studies that indicate infection with herpes viruses, such as herpes simplex virus, may involve endothelium and by attracting granulocyte attention, be an important contributor to atherosclerosis.

In ancillary studies, Jacob and colleagues have demonstrated that other circulating white cells, namely lymphocytes, can significantly damage vascular endothelial cells, but only when activated by certain lymphocyte stimulants. Much interest has centered at the University of Minnesota in cancer therapy that uses LAK cells, which are mononuclear blood cells stimulated by the lymphocyte activator, Interleukin 2.

Jacob received his M.D. cum laude in 1958 from Harvard Medical School. His association with the University of Minnesota dates to 1968, when he was named chief of the Section of Hematology at the Medical School. He became a full professor of medicine in 1970. Jacob was a visiting professor of hematology at the Royal Postgraduate Medical School and Hammersmith Hospital in London in 1973-74. He was named vice-chairman of the Department of Medicine in 1987, and the same year became professor of pathobiology and laboratory medicine and pathology.



Horace H. Loh, Ph.D.

Horace H. Loh, Ph.D.

Dr. Loh was only recently appointed professor and head of the Department of Pharmacology at the University of Minnesota Medical School, assuming his duties in July.

He came to Minnesota from the University of California School of Medicine where he was a professor in the depart-

ments of psychiatry and pharmacology. For the past 10 years, Dr. Loh's research has been in the areas of neuropharmacology and biochemical pharmacology. Specifically, he has focused on the neurochemical mechanism of narcotic actions; opioid receptor identification, purification, and cloning; and the pharmacology of endorphins.

His MERIT award was granted for a project entitled "Structural and Functional Studies of Mu Opioid Receptor." Dr. Loh has been involved in research to characterize and clone opioid receptors from the brain for many years. Recently, he has purified an opioid receptor from bovine brain that has selectivity for mu (morphine-like) opioids.

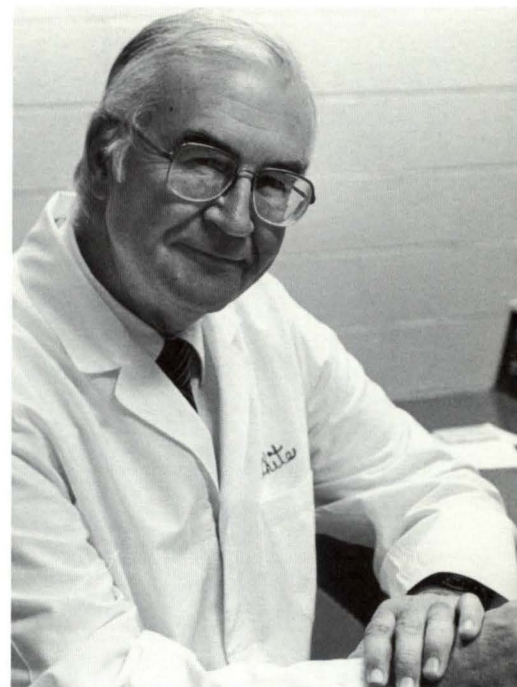
One of the important findings of Loh's research, thus far, has been that lipids are necessary for this opioid binding. "Neither the receptor protein itself, nor any lipids that we have tested, exhibit significant opioid binding by themselves," notes Loh. "However, in combination, high levels of binding are observed. Our recent work indicates that the lipid requirements include an acidic, polar head group, and fatty acid chains with two or more double bonds. The unsaturated fatty acids alone can also confer high levels of opioid binding on the receptor protein."

Loh received his B.S. in agricultural chemistry from the National Taiwan University in Taipei, and his Ph.D. in biochemistry from the University of Iowa School of Medicine. He was with the University of California School of Medicine from 1970 to 1988, beginning as a lecturer and research associate and rising through the ranks to full professor. He has also held positions as chief of the Drug Dependence Research Center at Mendocino State Hospital and associate professor of biochemical pharmacology at Wayne State University.

Loh has received numerous research awards including both the Career Development Award and the Research Scientist Award from the U.S. Public Health Service and West Germany's Humboldt Award for senior U.S. scientists.

James G. White, M.D.

Dr. White has had a distinguished career in the fields of pediatrics and laboratory medicine and pathology. His accomplishments were acknowledged in 1984 when he was named a University of Minnesota regents' professor of pediatrics and labo-



James G. White, M.D.

ratory medicine and pathology, in 1987 when he received the Distinguished Career Award for Contributions to Hemostasis, and again in 1988 when he was selected for an NIH MERIT award.

Investigations in White's laboratories are directed toward the development of knowledge on blood platelet function in normal hemostasis; the blood platelet's role in the pathogenesis of inherited and acquired bleeding disorders; and the contribution of blood platelets to vascular injury, thrombosis, and atherosclerosis. White's research team combines physiology, biochemistry, pharmacology, immunology, engineering, biophysics, and morphology in a total approach to understanding platelet structure, function, and pathology.

White received his medical degree from the University of Minnesota in 1955. After a rotating internship at the Detroit Receiving Hospital and a stint in the Army, Dr. White returned to the University of Minnesota in 1958 for his pediatric internship and residency and has remained here since then. He was named an assistant professor of pediatrics in 1963, associate professor in 1966, and full professor in 1970. He became a professor in laboratory medicine and pathology in 1984. In addition to his many other responsibilities, White was appointed associate dean for research in the Medical School in 1985.

White serves on the editorial boards of six scientific journals and has written more than 400 manuscripts on his research.



PRACTICING REAL MEDICINE:

THE UMD PRECEPTORSHIP

PROGRAM

MEDICAL STUDENTS
LEARN FIRSTHAND
ABOUT THE JOYS
AND FRUSTRATIONS
OF LIFE AS A FAMILY
PRACTICE PHYSICIAN
IN A RURAL AREA.

By Patricia Miller



Preceptee Mary Vomacka.

It hadn't been an easy 24 hours for Mary Vomacka.

The second-year medical student at the School of Medicine, University of Minnesota, Duluth, looked exhausted as she sipped some early morning coffee in the doctors' lounge at the Grand Rapids Hospital. She had spent the last three days witnessing and experiencing the rewards and trials of a family doctor practicing in a small town.

It had been a long, emotionally draining night on call at the hospital's emergency room, a night during which she assisted Dr. Scott Gerling of Grand Rapids in treating a number of patients for

everything from heart attacks to terminal cancer. Two of those patients died, and Vomacka was present in the early morning hours when Gerling informed the patients' families of the deaths.

"They tell you in class how it will be to confront and inform the families of a death. But to see someone do it with such sensitivity taught me even more," Vomacka says.

She is one of 48 second-year students (preceptees) from the School of Medicine matched with family practitioners (preceptors) in rural communities — many no more than a wide spot in the road — as part of the school's Family Practice Preceptorship Program. Throughout the year, second-year students spend three, three-day sessions with their preceptors, shadowing the physicians' every move and even living with their families as members of the rural community.

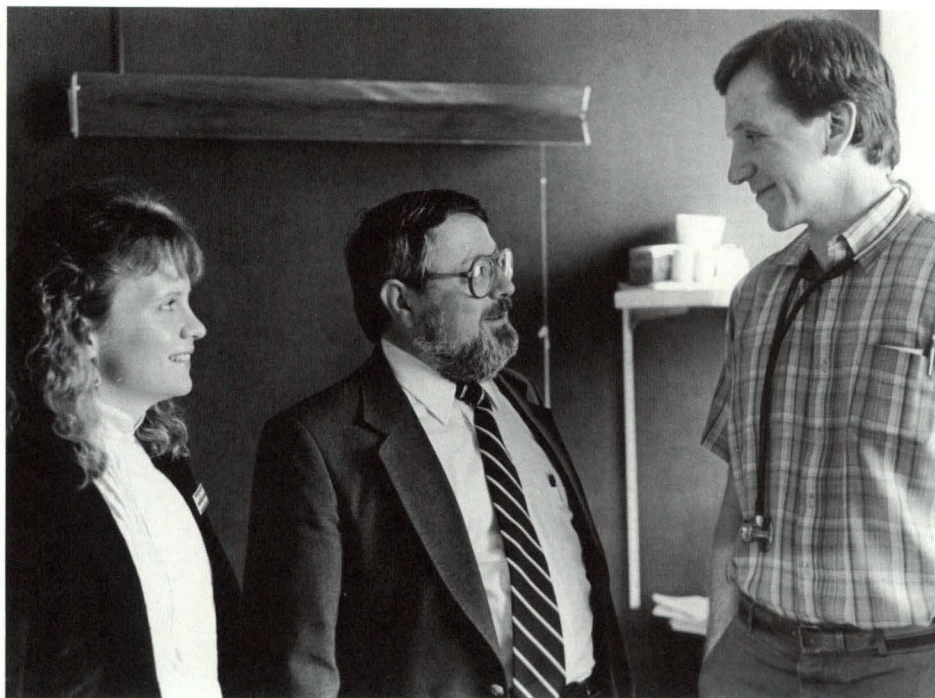
Vomacka had spent the previous day with Gerling at the North Star Clinic in Grand Rapids, where she assisted him with patient treatment, and from there had proceeded to on-call at the hospital emergency room. After a busy night, she and Gerling were headed back for another day at the clinic. There hadn't been much sleep, just what she could grab on a lumpy sofa in the lounge between seeing patients, but then Vomacka wasn't in Grand Rapids to sleep. She wants to become a family doctor and she was there for a brief, but realistic glimpse of what her future holds.

"It's been a hectic 24 hours of medicine," Gerling said as he joined Vomacka in the doctors' lounge. "It was very intense, but pretty much a typical hard day as a family practitioner, although it's a relief that every day is not like this."

Gerling, himself an alumnus of the School of Medicine who did his preceptorship in Grand Rapids, says he has positive feelings about his life as a family practitioner, his medical education at UMD, and his six years as a preceptor.

"The whole concept of what the School of Medicine is doing with rural physicians is wonderful and a sign of its commitment to getting good people to become family practitioners," Gerling says. "And students are given the opportunity to discover that there is good medicine practiced in rural areas."

The preceptorship program began in



Preceptorship program director James G. Boulger (center) discusses the program with preceptee Mary Vomacka and Scott Gerling, M.D., of the North Star Clinic in Grand Rapids. Every year, Boulger personally visits each of the 48 preceptorship sites throughout Minnesota.

1972, the same year the School of Medicine opened. Started from a concept conceived by Charter Dean Robert Carter and William Jacott, presently assistant vice president of Health Sciences at the Twin Cities campus, the program has continued since 1973 under the direction of James G. Boulger, currently the school's interim dean, and Thomas Day, M.D., director of the Family Practice Residency Program in Duluth. Boulger oversees the second-year students — matching students to physicians and communities — and Day monitors first-year students, who participate in ten half-day preceptorship sessions with Duluth, Proctor, and Cloquet physicians.

"Our students experience professional life in a small community and have the opportunity to see the benefits, as well as the problems, inherent to the practice of medicine in a rural setting," Boulger says, emphasizing that the program is designed to expose students to the practice of family medicine, not necessarily to teach them how to practice medicine.

The School of Medicine was estab-



Preceptee Anita Strei examines Floyd Knox, a patient at the Northland Medical Center in Bigfork, Minn.

lished with the primary mission of encouraging future physicians to enter family practice in rural communities, and the preceptorship program assists in fulfilling that goal.

"Being a preceptee acts as a large reinforcer for students considering family practice, although it does not necessarily change the mind of the student who has decided not to enter family practice,"

Boulger says. "It's usually a very positive experience that shows students how good family practice can be in a small community. They get a chance to see physicians out there practicing good medicine and enjoying it."

Preceptors, many who are former School of Medicine students, are chosen based on their location, the amount of clinical activity in their practice, reputation, and partners. Preceptors are not paid for their participation, but are given a clinical appointment at the School of Medicine. This year, students were placed in small communities throughout an enormous geographical area covering more than 45,000 square miles from Fargo, N.D., to Ashland, Wis., and from International Falls to Fairmont, Minn.

"The job of a preceptor is fun," Boulger says. "It's always enjoyable to be a good teacher and it's a good form of

"Students are given the opportunity to discover that there is good medicine practiced in rural areas."

continuing medical education for the physicians. The questions the students ask force the physicians to ask themselves why certain things are done or certain drugs are used."

And physicians are eager to participate in the program because of a tradition of giving within the medical profession — giving generously of themselves not just to patients, but to those coming up the ranks of the medical education system.

For Heidi Korstad, M.D., a former School of Medicine student practicing at the Northland Medical Clinic in Bigfork, a stereotypical one-horse town in northern Minnesota, her five years as a preceptor have been a way to pass on what she has learned and encourage a future family physician.

"Somebody was nice to me and kind enough to take an interest when I was a second-year student," Korstad says. "It was the high point of my second year, and it was so good to do clinical work after all the books."

Korstad and preceptee Anita Strei had spent the past three days seeing patients and treating the usual retinue of complaints and problems the family doctor faces on a regular basis.

"I have seen everything from hypertension and earaches to the common cold and even scrubbed and assisted with a vasectomy. Everything walks through the door here. It's real medicine," Strei says of her time at the clinic, a modern facility that serves Bigfork and several surrounding communities as clinic, hospital, nursing home, x-ray center, and laboratory. And Kent Johnson, preceptee for George Rounds, M.D., also on staff in Bigfork, echoes Strei's impression of a number of different medical situations seen at the clinic.

"There is such a variety of patients, from infants to the elderly," Johnson says. "We are dealing with everything from the common cold to terminal can-



Preceptee Rodney Hayes examines a patient with a ganglion cyst at the Brainerd Medical Center.

nized in the grocery store to a patient painting a physician's house when he can't directly pay the medical bills. Students even discover that there are still physicians that make house calls.

"I try to show students how I live and what I do in my spare time — we go hunting and fishing, things you don't do in the city — but I also show what I do and how I relate to my patients on a personal basis," says Korstad, adding that there aren't many physicians' offices where a 10-point buck can be seen walking just a few feet from the office window.

Students also experience the small town atmosphere and the feeling of being part of a close-knit community where physicians find their medicine easier to practice because of the close contact they have with patients and their families.

"I see all aspects of Dr. Lewer's life — his practice and his home life, the good

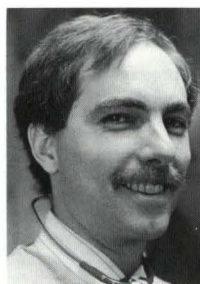
"The questions the students ask force the physicians to ask themselves why certain things are done."

cer. This really gives us a taste of what to expect in the profession."

Preceptees usually are given hands-on opportunities to perform initial patient examinations, after which they consult with the physician on possible diagnoses and see the patient a second time with their preceptor.

"It's an opportunity for students to push off the edge and see patients by themselves. For me, that was the most frightening part of being a preceptee, doing the procedures, the pelvic exams, the stitches, but those things are so important when learning about the common sense, non-academic, family practice approach to medicine that doesn't deal with all patients through tests and drugs," Korstad says.

Students also are given an opportunity to see the lifestyle of the family physician — a lifestyle differing widely from that of a specialist in a large city — which includes everything from being recog-



Preceptor Mark Gray, Lake Region Clinic, Brainerd.

"This is an excellent program for those of us who are disconnected from medical education. It keeps us in touch with academics and the students."



Ann Martin, preceptee for Mark Gray, M.D., Lake Region Clinic, Brainerd.

"It's good to see the family life of the physician and see how he practices medicine in a rural setting, the techniques he uses, and how he deals with patients. I've also

seen several of the same patients I saw the last time I was here, and that's a real example of the continuity of care provided by the family practitioner."



Anita Strei, preceptee for Heidi Korstad, M.D., of the Northland Medical Clinic, Bigfork, Minn.

"Everything comes in the door here. It's real medicine and gives you a feel for the real world and real patients."



Rodney Hayes, preceptee for Peter Dunphy, M.D., at the Brainerd Medical Center.

"I have been mulling over family practice for some time. The preceptorship has shown me the variety and the broad scope in terms of medical practice,

and the bad, the time commitments, the patient load. It gives me an idea of what it will be like when I am out there practicing," says Roger Hynes, preceptee for Greg Lewer, M.D., of the Cayuna Range Clinic in Crosby, Minn. "He is the type of doctor I saw when I was growing up, and this experience helps me see the good things about this sort of life. We learn about dispensing medicine in the classroom, but we come here and see how it is put into practice."


At the Lake Region Clinic in Brainerd, it's 2 p.m. when a delivery man brings a pizza through the waiting room. A few minutes later, preceptee Ann Martin and preceptor Mark Gray, M.D., are munching on a late lunch after a morning of seeing patients. Martin, who is single, is discovering the demands made on the time of a family practitioner, like Gray, who is married and the father of three.

"I've thought about the time commitment, but seeing the lifestyle, I think I can balance a career with a family life," Martin says. "The hours and on-call can be long, and things can get repetitious, but at the heart of everything is the continuity of care for patients."

She also is learning about the humanitarian aspects of medicine from Gray as she takes patient histories and assists with medical procedures and physical examinations.

"I try to share the personal aspects of medicine, as well as the technical aspects, such as how to talk to patients, listening, touching, and really getting to know the patients because each one is different and brings different challenges. It's important to know what is going on in their lives," says Gray, who has been a preceptor for six years and also is an alumnus of the School of Medicine.

For the second-year students, the preceptorship program also offers a break from class work and books and personalizes their medical training.

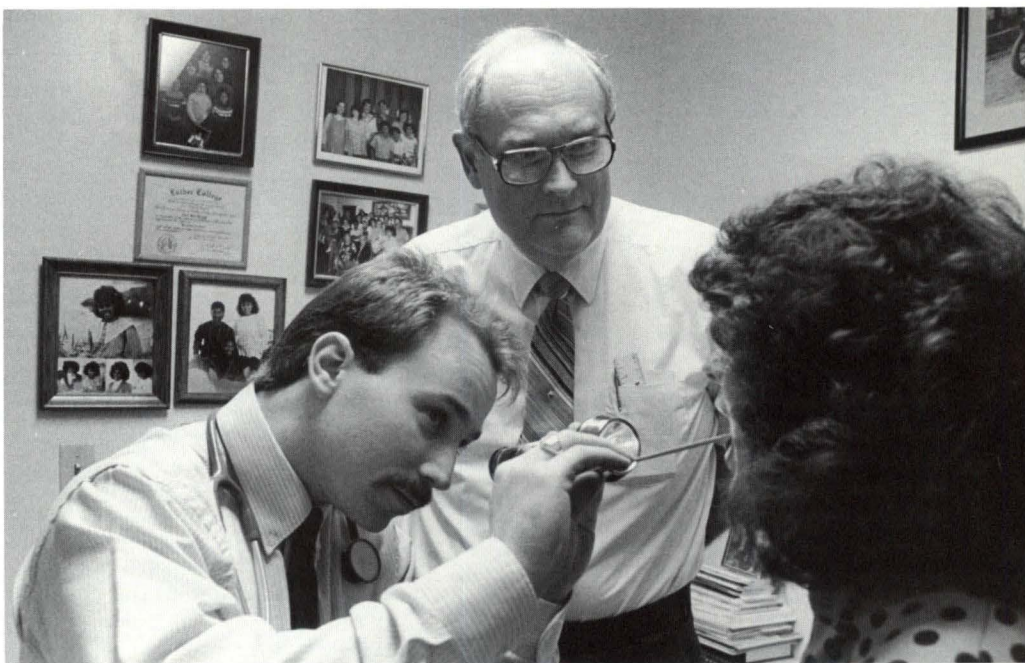
"It's like a light at the end of the tunnel — your first opportunity to see yourself as a physician and that's what you're striving for," Korstad says. 

Patricia Miller is senior information representative at the University of Minnesota, Duluth, School of Medicine.



Preceptee Ann Martin assists preceptor Mark Gray, M.D., in his examination of cancer patient Derald Watson of Grand Rapids.

"It's an opportunity for students to push off the edge and see patients by themselves."



Preceptee Jay Knaak conducts a patient examination under the watchful eye of preceptor Carl Griesy, M.D., of Two Harbors. Griesy has participated in the School of Medicine program since its beginning in 1972.

Medical School Graduation: A Centennial Celebration

Graduation Day had special significance this year, for the Class of 1988 was the 100th class to graduate from the University of Minnesota Medical School. June 3 marked the culmination of four years of hard work for the 270 medical students who received their degrees at a stirring commencement ceremony highlighted by awards, speeches, and the oath for new physicians.

Nadine Smith, M.D., vice president of the Minnesota Medical Foundation, recognized the recipients of awards sponsored by MMF: **Joanne Hilden**, MMF Undergraduate Research Award, **Darla Granger**, **Sarah Kaus**, **Jon Ritter**, and **Michael Swenson**, MMF Medical Student Achievement Awards; **Joanne Riley** and **Lisa Lund**, Nicollet Clinic Founders Scholarships; **David Edwards**, American Cancer Society Scholarship; **David Kendall**, Richard C. Horns Memorial Award; **Hila McCoy**, George E. Williams Scholarship; **Marie Welshinger**, Daniel A. Coyle Memorial Award; **Joanne Hilden**, **Pamela Jensen**, **Desiree Kempcke**, and **Naomi Olson**, Ruth Boynton Memorial Scholarship; and **Grant Burch**, Nicolette Norton Memorial Scholarship.

Other award-winning graduates included: **Brian Bunkers**, Southern Minnesota Medical Association Outstanding Senior Award, and **Joanne Riley**, Maxine Nelson-AEI Foundation Award.

Two honorary doctor of science degrees were awarded this year, to **Lester Breslow** and **Earl E. Bakken**. Dr. Breslow received his M.D. degree from the University of Minnesota in 1938 and a master of public health in 1941. He is known for his pioneering work on the relationships between physical health and health practices. He has also been a major proponent of disease prevention strategies. Earl E. Bakken is founder and senior board chair of Medtronic. He received a degree in electrical engineering

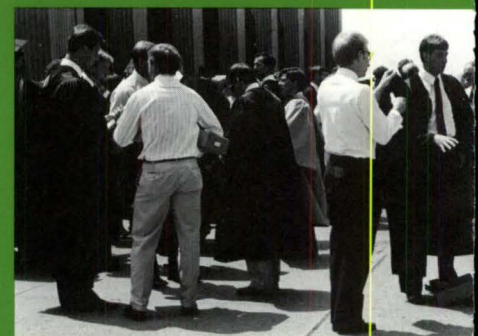
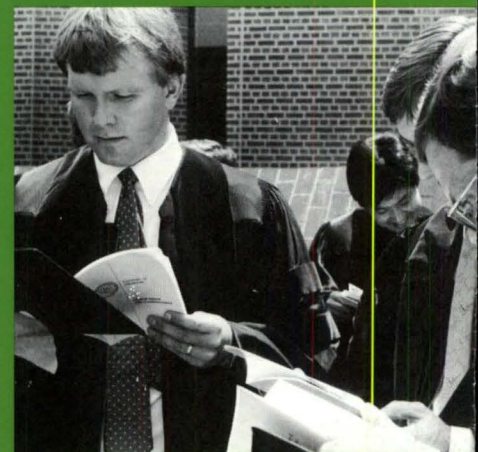
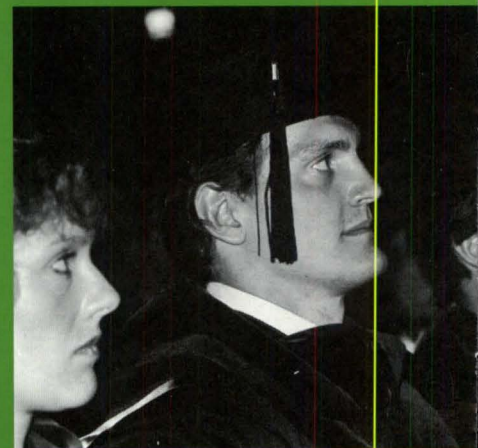
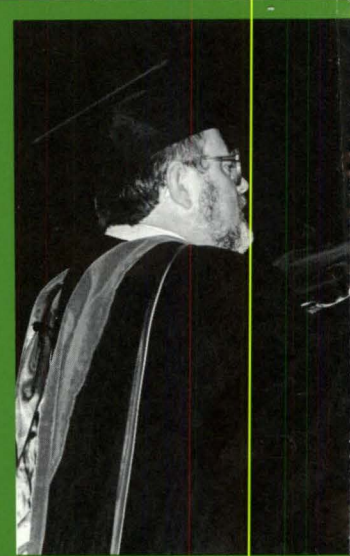
from the University of Minnesota in 1948. In the 1950s, he worked with University surgeons C. Walton Lillihei and Richard L. Varco to develop the world's first wearable, battery-powered cardiac pacemaker.

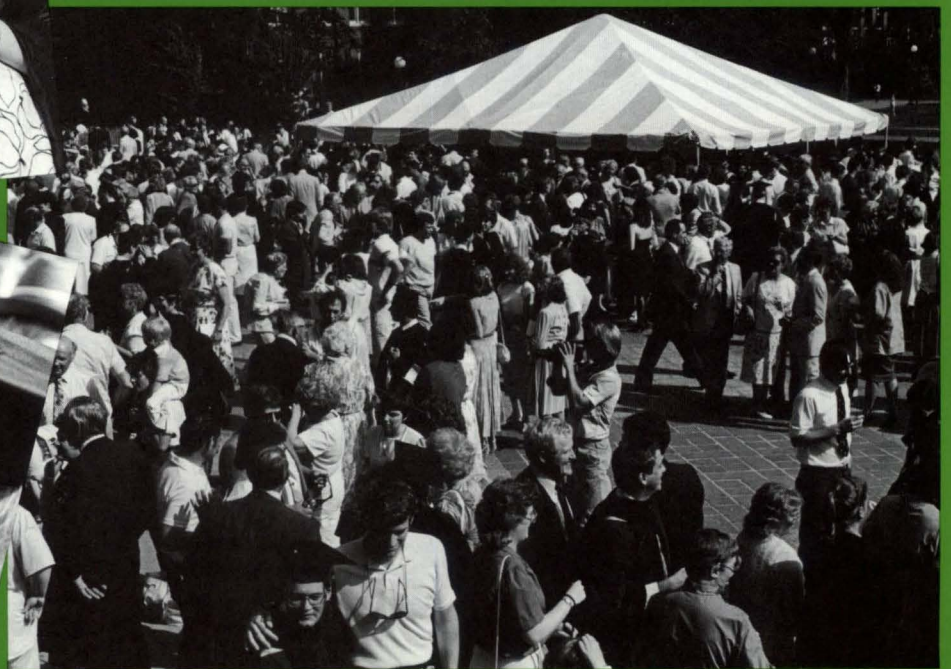
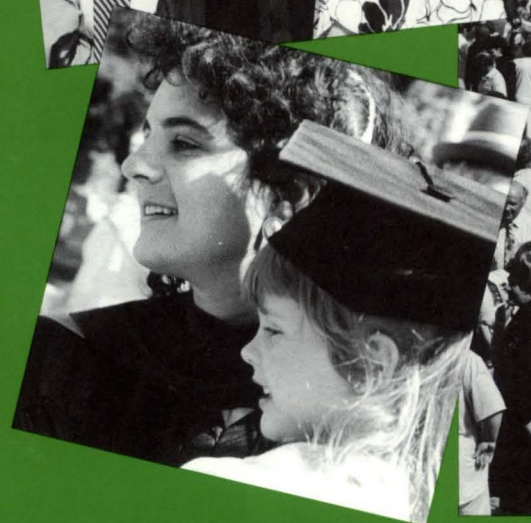
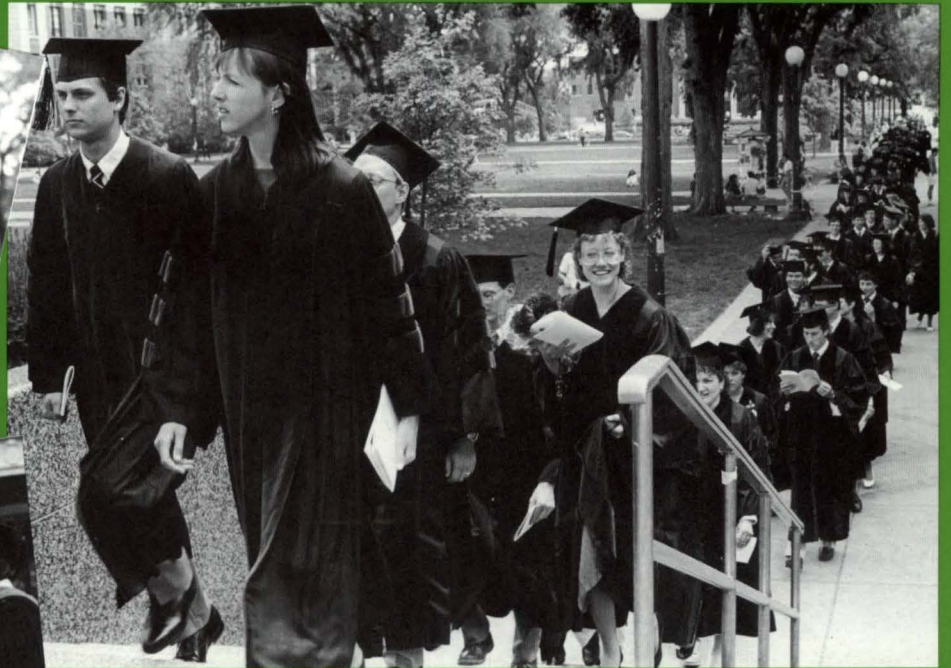
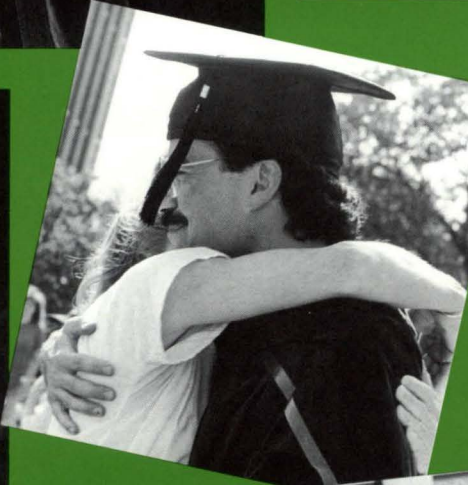
Following the conferring of degrees by Neal A. Vanselow, M.D., vice president for Health Sciences, class president Sarah Kaus spoke on the subject, What is Success? She listed the key steps to success in the field of medicine as responsibility to patients, motivation and the genuine desire to help people, and artistry — the importance of the human element along with technical skills.

Speaker Arnold S. Relman, M.D., editor of the *New England Journal of Medicine*, addressed the extraordinary changes occurring in the profession of medicine. Four things impacting this situation are: the rapid acceleration of scientific and technical advances in medicine, while the need for attention to the whole patient is greater than ever before; the fact that we are moving for the first time in this country into an era of limited resources; the situation resulting from the decline of fee-for-service type of practice; and the increase of public scrutiny of the medical profession.

Relman offered three guidelines to the graduating physicians to deal with these changes. He suggested that they be ever mindful of the basic ethical underpinnings of their chosen profession, which is to serve their patients' needs; that they accept the obligation to be technically competent and intellectually alive; and that they become socially responsible, participating in programs of assessment of the medical field.

Following the ceremony, the graduates joined with colleagues, friends, and families at a reception in front of Northrop Auditorium to offer congratulations, best wishes, and goodbyes. ☂





MEDICAL SCHOOL NEWSBRIEFS

Excitement, surprises at Match Day

There were screams of joy, looks of dismay, and even a few tears as fourth-year students at the University of Minnesota Medical School ripped open their envelopes to discover where they would be spending the next few years of their lives.

It was all a part of the National Resident Matching Program on March 23. The envelopes revealed where these graduating medical students would spend their residencies. The Matching Program matches medical students with the available resident positions in hospitals throughout the country. Students rank their choices of residencies, and institutions, in turn, rank their preference of candidates. The computer does the rest.

At the University of Minnesota, 253 students participated in the match out of a nationwide total of more than 16,000. Nearly 95 percent of Minnesota's students were matched, with 58.1 percent receiving their first choice of resident positions, 15.8 percent their second



Fourth-year students congratulate each other on Match Day.

choice, and 7.5 percent receiving their third choice.

This was the first year of the decade that the number of students matched into family practice nationwide decreased — down 16 percent over 1987. At Minnesota, family practice was the second most popular specialty with 19.3 percent of the students selecting it. Medicine was the

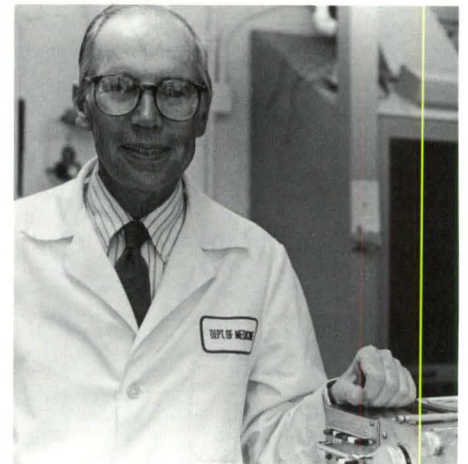
number one specialty with a 24.8 percent match rate. Surgery was third at 11.3 percent, followed by pediatrics, transitional, psychiatry, obstetrics/gynecology, orthopaedic surgery, anesthesiology, pathology, radiology, emergency medicine, and urology.

Nearly half (49 percent) of Minnesota's graduating class will remain in the state for their residencies. More than 25 percent will be at the University of Minnesota Hospital and Clinic, 10.2 percent at Hennepin County, 6.8 percent at Mayo, 3.4 percent at Abbott Northwestern, 1.8 percent at St. Paul Ramsey, and 1.5 percent at Duluth. □

Dr. Tobian receives award for hypertension research

Dr. Louis Tobian, University of Minnesota professor of medicine, received the International Society of Hypertension's top award, the Volhard Award, May 23 in Kyoto, Japan.

Tobian was honored by the society, the world's leading high blood pressure association, for his lifetime achievements. He is internationally renowned for his accomplishments in hypertension research, which range from the discovery that arteries affected by high blood pressure contain extra sodium to the idea that a diet high in potassium can provide protection against strokes and kidney and artery disease for those with high blood pressure. He has been at the University since 1954. □



Dr. Louis Tobian

Dr. Levitt given Distinguished Service Award



Dr. Seymour Levitt

Dr. Seymour R. Levitt, University of Minnesota professor and head of therapeutic radiology, received the University of Colorado Distinguished Service Award

May 28 in Boulder, Col. The award is given to those whose outstanding achievements and contributions are of particular importance to Colorado or the nation.

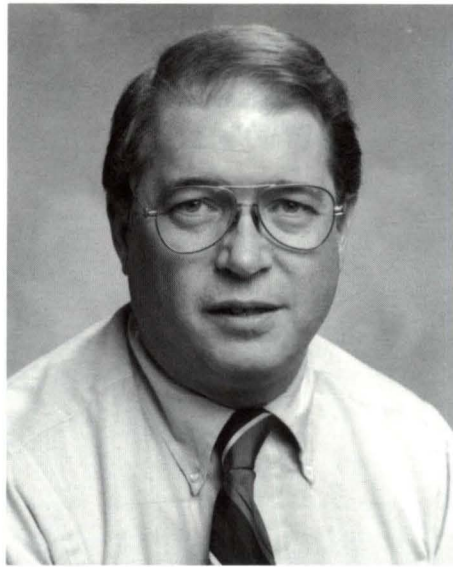
Levitt, an international expert in lymphoma and breast cancer treatment, received a bachelor's degree from the University of Colorado in 1950 and a medical degree in 1954, also from Colorado. He has been at the University since 1970.

Levitt has also delivered several talks abroad recently. These have included a presentation on clinical trials and lung cancer at the radiology diagnostic conference at the Catholic University of Rome Medical School; a speech on breast cancer at the Hadassah Hospital in Jerusalem; a presentation before cancer specialists and radiologists from throughout West Germany on brachytherapy, gall bladder cancer, and brain tumor implants in Rothenberg, West Germany; and a major address at a plenary session in Seoul, South Korea, concerning cancer immunotherapy and breast cancer. □

Dr. Nesbit wins JLM Community Volunteer of the Year Award

Dr. Mark Nesbit, University of Minnesota professor of pediatrics, therapeutic radiology, and nursing, and section head of pediatric oncology at the University of Minnesota Hospitals, was named Community Volunteer of the Year by the Junior League of Minneapolis at its May 1988 annual meeting.

Nesbit was one of the original fundraisers for the Twin Cities' Ronald McDonald House. He was also the developer of and trainer for CARE (the Children's Cancer Awareness Research and Education project) which provides volunteer support for families of children undergoing treatment for cancer-related illnesses at the University of Minnesota Hospitals.



Dr. Mark Nesbit

He currently serves as the national vice chairman of the Children's Cancer Study Group, and he sits on the board of directors of the American Cancer Society, the Combined Health Appeal (CHA), and the Children's Cancer Research Fund (CCRF). □

Dr. Van Beek participates in US/Soviet symposium

Dr. Allen L. Van Beek, clinical assistant professor at the University of Minnesota Medical School, Department of Surgery, and director of microsurgery at North Memorial Medical Center, traveled to the Soviet Union with five other prominent American surgeons in June to participate in the first bilateral symposium between the United States and the Soviet Union on plastic and reconstructive microsurgery.

"The sharing of medical knowledge and techniques by American and Soviet doctors is not a political event," says Van Beek. "It is a step toward improving medical treatment in our two countries and throughout the world."

A graduate of the University of Minnesota Medical School, Van Beek is the recipient of many awards in his profession.

According to Van Beek, papers delivered at the symposium covered such topics as microsurgical approaches to the reconstruction of bones and soft tissues, peripheral nerve repair, and major limb, thumb, and digital replantation. The American physicians also had the opportunity to visit Soviet operating theaters to observe Soviet surgical techniques. □

Dr. Ferris elected Association of Professors of Medicine president

Dr. Thomas F. Ferris, Nesbitt professor and chairman, Department of Medicine, has been elected president of the Association of Professors of Medicine. This organization represents the chairmen of departments of medicine in the 127 medical schools in the United States. □

Dr. Cohn honored with prestigious award

Dr. Jay N. Cohn, professor of medicine and head of the Cardiovascular Division, was awarded The Sir Thomas Lauder Brunton Award in a ceremony in Montreux, Switzerland, on April 14.

The award is presented jointly by the Geriatric Cardiology Research Foundation and Schwarz Pharma and is named for the physician who in 1867 first reported the use of nitrates for the treatment of cardiac pain. Cohn was honored for his role in demonstrating life-prolonging effects of nitrates in the management of congestive heart failure. He served as organizer and chairman of a Veterans Administration Cooperative Study (V-HeFT) that showed for the first time that vasodilator drugs could reduce mortality in patients with heart failure. □

Second-year students test clinical skills

Second-year medical students put their classroom learning to work in early May, participating in an unusual test of their bedside skills called the Objective Structured Clinical Evaluation (OSCE).

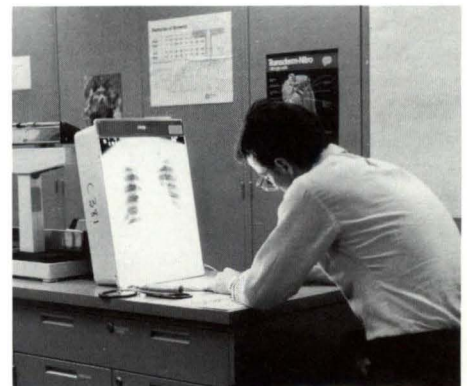
The format consists of approximately 20 stations, where students conduct a variety of real-life clinical situations such as listening to a patient's heart, studying x-rays, performing a well-baby exam, or counseling a patient on smoking cessation. Students are permitted only five minutes at each station, and at the sound of a whistle rotate to their next stop.

In a situation unique to the University of Minnesota, the "patients" for the OSCE were third- and fourth-year medical students who volunteered their services for the day. Over 100 responded to the request for volunteers, saying that the experience helped them know how it feels to be a patient, and fine-tuned their own evaluation skills.

Second-year medical students traditionally take only written exams to test their knowledge of physical examinations, but this year the Medical School received a grant to try the OSCE. The experiment will help guide decisions on how to improve the Medical School curriculum. More than 180 second-year students participated.

Only about 20 medical schools around the world have used the OSCE, with the majority of those located in Canada or Europe. The test was developed in New Zealand 10 years ago.

Medical School departments participating in the OSCE included family practice, medicine, pediatrics, and neurology. □



Second-year student evaluates an x-ray.

University study links menstrual cycle and breast cancer treatment

A woman's menstrual cycle may determine the best time for breast cancer tumor removal and may influence whether the cancer will spread, according to University of Minnesota medical oncology associate professor William Hrushesky.

In a presentation March 23 at the American Cancer Society Science Writers' Seminar in Daytona Beach, Fla., Hrushesky said that in studies of female mice, 40 percent of the mice with breast cancer whose tumors were removed near the fertile part of their reproductive cycles were disease-free at the cancer's original site 28 days later. Only 16.4 percent of those whose tumors were removed in their infertile phase were cancer-free in the same area after the same amount of time.

When the lungs of the mice were checked for metastases, or spreading of the cancer, 27 percent of the mice whose tumors were removed during the fertile phase were free of cancer, compared with only 12.3 percent for the other group. Menstrual cycles in women and estrous cycles in mice are responsible for precise, coordinated releases of sex hormones.

"Human and mouse breast cancers are often very responsive to body concentrations of sex hormones," says Hrushesky. "Depending on the concentration, the breast cancer can totally disappear for many years." Normally, in human breast cancer, chemotherapy is given following tumor removal, and it generally increases long-term survival by about 10 percent. "If what is true for these mice is true for cycles in women, our findings indicate that the timing of the initial surgery alone could potentially be responsible for much more than a 10 percent survival increase — perhaps two or three times more," says Hrushesky. "We have already begun a retrospective clinical study to see if this is true for women's cycles. I hope that this study's results can be used for human breast cancer treatment."

Hrushesky's co-investigators for this study were Helen Ratajczak of the Illinois Institute of Technology Research Institute, Chicago, and University of Minnesota medical oncology scientist Robert Sothern. □



Dr. William Hrushesky

Institute of Human Genetics receives awards

All University biologists will benefit from new automated instrumentation being purchased by the Microchemical Facility of the Institute of Human Genetics. Thanks to awards totalling \$248,000, the facility is adding an automated peptide synthesizer, a protein microsequencer, and a high-performance liquid chromatograph. The awards were from the National Institutes of Health's Shared Instrumentation and Small Equipment Programs; the National Heart, Lung and Blood Institute's program for Shared Research Facilities for Molecular Biology; and the Leukemia Task Force.

The Institute of Human Genetics has also received a grant of more than \$1 million from the National Institute of Allergy and Infectious Diseases. The five-year grant will enable the institute to develop an animal model for papillomavirus (PMV) infection. Among other things, the model will be used to test antiviral drugs against PMV. Principal investigators Anthony Faras and Ronald Ostrow have spent several years studying the virus, which is sexually transmitted and causes benign tumors that may progress to cervical cancer. □

University microbiologist patents Lyme disease vaccine

Dr. Russell Johnson, professor of microbiology at the University of Minnesota Medical School, has received a patent for a vaccine to provide immunity to Lyme disease. He is also developing a urine test to detect the disease.

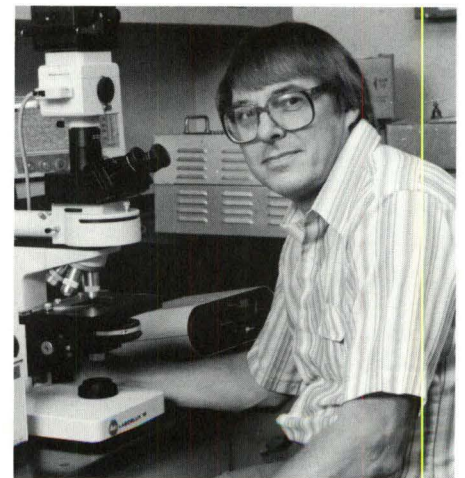
Johnson has been studying the Lyme disease bacterium — a spirochete called *Borrelia burgdorferi* — for about six years, and has become a well-known authority on the subject. He has lectured on Lyme disease throughout Minnesota and the United States, has appeared at conferences in South America, and plans trips in the near future to Switzerland and Czechoslovakia.

Johnson's lab is also evaluating drugs that are being tested in Minnesota, Boston, and Old Lyme, Conn., where Lyme disease was first identified in 1982.

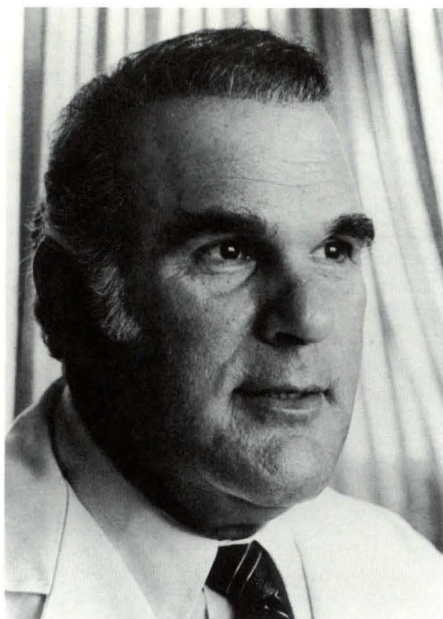
Transmission of Lyme disease is through the bite of the deer tick, which is about two-thirds the size of the wood-tick. Symptoms of the disease include an expanding red rash, followed by flu-like complaints such as headache, chills and fever, joint and muscle aches, and stiff neck. Multiple symptoms may develop, making diagnosis difficult.

The deer tick is becoming increasingly prevalent in Minnesota, one of seven states with the highest incidence of Lyme disease. The other states are New York, New Jersey, Massachusetts, Connecticut, Rhode Island, and Wisconsin.

Johnson noted that it will be several years before the vaccine is fully tested and available to the public. □



Dr. Russell Johnson



Dr. John S. Najarian

Dr. Najarian elected president of American Surgical Association

Dr. John S. Najarian, University of Minnesota regents' professor and head of surgery, has been elected president of the American Surgical Association. He will serve for one year.

The association's presidency is regarded as the highest honor that can be bestowed on an American surgeon. Past presidents include William and Charles Mayo and former University surgery head Owen Wangenstein. Founded in 1880, the association is a select professional and scientific society of surgeons elected by their peers. It publishes the journal *Annals of Surgery*.

Najarian's election was in San Francisco May 4. □

Bone Marrow Transplant Program receives grant

The Bone Marrow Transplantation Program has received a four-year renewal grant from the National Cancer Institute. NCI awarded the program \$1.24 million to cover the interdepartmental work of 29 researchers for the year beginning March 1988. Professors John Kersey and Norma K.C. Ramsay are principal investigators for the project.

The grant supports the major part of the bone marrow transplant research program which includes pediatrics, medicine, laboratory medicine, pathology, and radiation therapy. □

Medical School faculty appointments announced

Three key faculty appointments have been announced at the University of Minnesota Medical School. They include: Henry J. Griffiths, professor, Department of Radiology; Arthur J. Matas, associate professor, Department of Surgery, and Robert F. Miller, professor and head, Department of Physiology.

Dr. Henry Griffiths has served as professor of radiology at the University of Toronto and radiologist-in-chief at Toronto General Hospital since 1986. From 1981 to 1986 he was professor of radiology and senior radiologist at the University of Rochester School of Medicine and Dentistry, New York. He previously served as an associate professor of radiology and associate professor of orthopaedics at that same institution. Griffiths was also a former faculty member at Harvard Medical School and Tufts University. His medical degrees, residency, and specialty training were undertaken in London. Griffiths is the author of some 70 publications and five books and has presented numerous lectures and papers.

Dr. Arthur Matas earned a B.Sc. degree and an M.D. in 1972 from the University of Manitoba. He has been a faculty member at the Albert Einstein College of Medicine and Montefiore Medical Center, New York, since 1981, initially as an assistant professor of surgery with promotion to associate professor in 1986. He formerly served on the faculty at the State University of New York Downstate Medical Center for one year. Matas served his internship and residency in surgery at the University of Minnesota Hospital and held a fellowship in transplantation in 1979-80. He is a highly regarded transplant surgeon, and will be involved with the direction of the clinical kidney transplant service, patient care, the teaching of medical students and fellows, and research.

Dr. Robert Miller has been recommended to fill the Bert Cross/3M Chair in Neurosciences. He has been a faculty member at the Washington University School of Medicine, St. Louis, since 1978. He presently is a professor of cell biology and physiology, neurobiology, and ophthalmology. Miller previously served on the faculty at the State University of New York, Buffalo, for seven years, first as an assistant professor of

Anniversary plans underway

Plans are accelerating for the upcoming anniversaries of the University of Minnesota Medical School and the Minnesota Medical Foundation. To be held concurrently from September 1988 through June 1989, the celebration will mark the 100th anniversary of the Medical School and the 50th anniversary of MMF.

Lectures, panel discussions, exhibits, and special publications will all be part of the event. Speakers will include such notables as C. Everett Koop and Ellen Goodman. Ms. Goodman, columnist for the Boston Globe, will join Dr. Arthur Caplan on September 23 for a discussion on a biomedical issue involving reproductive technology. Caplan is director of the University of Minnesota Center for Biomedical Ethics. Surgeon General Koop is scheduled for a spring lecture, and will speak on Health Issues for the 21st Century.

Prominently displayed in the corridors of the Phillips-Wangenstein building throughout the entire academic year will be exhibits for each Medical School department and for the Minnesota Medical Foundation. The exhibits, created and funded by 3M, will feature departmental histories as well as a look at the present and the future.

The Fall 1988 MMF Medical Bulletin will be a special commemorative edition, highlighting the history of the Medical School and MMF.

An all-class reunion is planned for June 1989, bringing alumni from throughout the country to celebrate three days filled with memorable activities. The weekend will include the Medical School graduation ceremony, reunions by class, and will culminate in a gala "Night Under the Stars," an evening of dinner and dancing on Northrop Plaza.

Watch for further details in the Fall 1988 Medical Bulletin, or call the Special Programs office at (612) 626-1987 for more information. □

physiology with promotion to associate professor in 1976. He earned a B.S. degree in biology from Utah State University, Logan, in 1962. In 1967 he was awarded an M.D. degree from the University of Utah College of Medicine. □

Minnesota researchers say aspartame safe

Fairly large amounts of the sweetener aspartame, known commercially as NutraSweet*, can be safely consumed daily by most healthy people, according to a University of Minnesota study.

In work conducted by epidemiology and nutrition professor Arthur S. Leon and pharmacology and medicine professor Donald B. Hunninghake, 108 healthy subjects ages 18 to 62 randomly received either placebo or 75 milligrams of aspartame for every 2.2 pounds of body weight with each meal for 24 weeks.

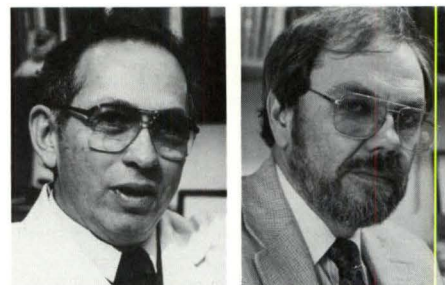
Leon and Hunninghake, who conducted the study under a grant from the NutraSweet Co., presented their work at the annual meeting of the Federation of American Societies for Experimental Biology (FASEB) in Las Vegas May 2.

To consume the same amount of aspartame taken by study subjects, a 154-pound person would have to drink 10 liters or 30 cans of an aspartame-

sweetened soft drink daily. The amount taken by those who took aspartame was one and one-half times the current recommended maximum daily consumption amount.

The subjects were evaluated every three weeks and no significant differences were noted between groups in resting heart rate, blood pressure, and body weight. Blood cholesterol levels and test results of kidney, liver, and blood cell functions were not significantly different between the groups. No known digestive products such as phenylalanine and methanol were accumulated by either group. Aspartame side effects reported in the past, including headaches, abdominal discomfort, and colds, occurred at about the same rate for both groups.

"The safety of aspartame has been confirmed in more than 100 human and animal studies," says Leon. "What is unique about our study is the large



Dr. Arthur S. Leon **Dr. Donald B. Hunninghake**

amount of aspartame that was administered for such a relatively long period of time. Using a dose one and one-half times the amount recommended by the Food and Drug Administration (FDA), the lack of significant side effects or blood or urine chemistry changes confirms the safety of this food additive for most people. In fact, the estimated current average daily consumption of aspartame is actually about one-tenth the amount administered in our study."

It is estimated that over 100 million Americans consume products sweetened with aspartame daily. □

*NutraSweet is a registered trademark of the NutraSweet Co.

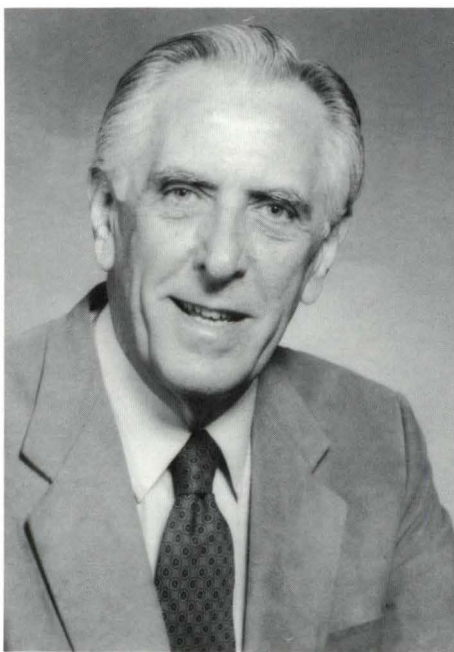
Dr. Kennedy address stresses aging of America

As the population of Americans most susceptible to cancer — those over 65 — continues to grow, oncologists need to prepare to better cope with this situation, says Dr. B.J. Kennedy, president of the American Society of Clinical Oncology. Kennedy, Masonic professor and head of oncology at the University of Minnesota, delivered his remarks at the society's annual meeting May 23 in New Orleans.

With the enlarging population of people over 65 years of age, there will be an increasing number of patients developing cancer. More than half of all cases of cancer are first diagnosed after age 65, and the chance of developing cancer continues to rise with increasing age. By 2011 the populations of Baby Boomers will reach 65 years of age, adding to the increased numbers of persons who will develop cancer.

Care given older cancer patients often differs markedly from that given younger patients because of attitudes concerning the treatment of older people held by family members and health care providers, Kennedy says.

"Older people often come to physicians with advanced cancer, due to the fact that they do not take advantage of cancer screening resources such as mammograms, pap smears, and stool blood



Dr. B.J. Kennedy

tests," says Kennedy. "They use fewer of these resources because Medicare often does not reimburse them for the costs involved, costs often unaffordable to those living on fixed incomes."

Older people are also offered possible cure of cancer less often by surgery, because many physicians feel older peo-

ple cannot tolerate surgery. Older persons are often excluded from clinical research trials, trials that can make a real difference in cancer survival, although the National Institutes of Health (NIH) now requires that NIH-sponsored research studies be free of age limits.

Due to the willingness of some physicians to give newer treatments to older patients, much higher survival rates have been achieved over the past 30 years for those with diseases such as acute leukemia, Kennedy says. Fear of possible complications from powerful treatments should not stop physicians from administering such treatments to older patients.

"Using the latest treatment techniques in combination with early detection methods can help oncologists help older people fight cancer while they still may have a chance," says Kennedy.

Since the number of older people is growing, there will be more older people dependent on health care. Kennedy stressed that more preventive measures need to be employed in order to have a better quality of life in later years.

Editor's Note: Dr. Kennedy has recently been named a regents' professor of medicine, the highest honor the University bestows on its faculty. □

MMF REPORT

Medical students elected to AOA

Alpha Omega Alpha (AOA) is a national medical honor society whose purpose is to promote scholarship, to encourage high standards in character and conduct, and to recognize high academic achievement. Election to AOA is a distinction that accompanies young physicians throughout their professional careers.

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

Students do not apply for election to AOA. Each year student members of the chapter, assisted by faculty advisors, apply the criteria set forth by the society to select students in their last two years of medical school. Academic excellence is not the only criterion for election: integrity, capacity for leadership, compassion, and fairness in dealing with one's colleagues are also given consideration in order to select those medical students who will most likely follow AOA's motto of "Worthy to Serve the Suffering."

Under the by-laws of the society, election 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.

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



Dr. Joyce Funke, who retired this year as treasurer of AOA, was thanked by David Teslow, MMF executive director, for the time and financial support she has given to AOA for 30 years.

Allert, Duluth; Kurt D. Anderson, Duluth; Bruce W. Arvold, Alexandria; Jeffrey A. Balke, Duluth; Blake A. Carlson, Minneapolis; John K. Erie, Crookston; Craig W. Florine, Madison Lake; Anne T. Goldschmidt, Montevideo; Margaret S. Gorbatenko, St. Paul; Sarah J. Ilstrup, Buffalo; Lisa A. Kline, Richfield; Kimberly J. Kramer, Wykoff; Lisa K. Lund, Chaska; Michael A. Lutarewych, Bloomington; Christopher J. McDevitt, Drexel Hill, Pennsylvania; Nancy H. Nelson, St. Paul; Lorre A. Ochs, Walker; Timothy A. Remple, Thief River Falls; Paul T. Rud, Bloomington; Jay J. Schantzen, Warren; Joseph B. Stanford, Provo, Utah; Scott D. Stenstrom, Hibbing; and Nancy J. Van Sloun, Minnetonka.

Initiates from the 1989 graduating class include: Mark C. Austin, Owatonna; Lisa M. Bucholz, Detroit Lakes; Rojer J. Day, Minneapolis; Lisa A. Drage, Rochester; Julie K. Drier, Minneapolis; Martin R. Engel, St. Paul; Paul S. Gotlieb, St. Paul; Jennifer L. Hillstrom, Woodbury; Robert C. Hoch, Minneapolis; Mark D. Holm, Cookato; Christopher A. Jackson, Deer Creek; Paul G. Johnson, St. Louis Park; Laura J. Johnston, St. Charles; Margaret A. Kirkegaard, Lakeville; Denise A. Larson, Willmar; Lawrence G. Mulhern, Fountain; Eric J. Olson, Edina; Nancy J. Perrizo, Benson; Todd T. Schlegel, Richfield; Wendy J. Shapiro, St. Louis Park; Paul J. Sovell, Marshall; Anne L. Weiss, Fridley; and Lori A. Witter, Mora. □

Campaign Update

As of early June, total gifts and pledges to the Minnesota Campaign stood at approximately \$340 million. The campaign topped its \$300 million goal in January.

The goal of creating 100 endowed chairs has been exceeded. With 114 new endowed faculty positions, the University now ranks among the top five public institutions in total number of these prestigious appointments.

The Medical School leads the University in number of new chairs and professorships. Included in this impressive list are: the Minnesota American Legion/Legion Auxiliary Brain Science Chair; the Earl E. Bakken Chair in Biomedical Engineering; the Frank E. Burch Chair in Ophthalmology; the Children's Cancer Research Fund Land Grant Chair in Pediatric Oncology; the 3M Bert Cross Chair in Neurosciences; the Catherine Mills Davis Biomechanical Engineering Land Grant Chair in Orthopaedic Surgery; the William F. Dietrich Chair in Fundamental Molecular/Cell Biology in the Basic Sciences; the Edwin Eddy Professorship in Neurocommunications Disorders; the John F. Finn Arthritis Foundation Land Grant Chair in Rheumatology; the Eugene Gedgaudas Professorship in Radiology; the Hazel O. Groves Professorship in Pediatric Dermatology; the Donald W. Hastings Chair in Psychiatry; the John B. Johnston Land Grant Chair in Neuroscience; the Helen and Milton Kimmelman Land Grant Chair in Immunobiology; the C. Walton and Richard C. Lillehei Land Grant Chair in Thoracic and Cardiovascular Surgery; the Elias Potter Lyon Research Professorship in Ophthalmology; the W.W. Allen and Elsa U. Pardee Chair in Cancer Biology; the Pennock Family Land Grant Chair in Diabetes Research; the Harold and Margaret Peterson Professorship in Neuroradiology; the Jay Phillips Chair in Surgery; the Harold G. Scheie Research Land Grant Chair in Ophthalmology; the Maurice Visscher Land Grant Chair in Physiology; the Owen H. and Sarah Davidson Wangenstein Chair in Experimental Surgery; and the Cecil J. Watson Land Grant Chair in Medicine. □



New members of AOA take the initiation pledge.

This year's initiates to AOA from the 1988 graduating class include: Debbie A.

MMF approves \$355,000 in research grants

The Minnesota Medical Foundation board of trustees approved \$355,000 in research and special grants at its spring quarterly meeting. The amount includes \$85,500 in faculty research grants, \$4,800 in student research grants, and \$263,506 in special grants for research equipment and salary support.

Faculty grants include: **Michael Basara, M.D.**, lab medicine and pathology, \$5,500 to research the role of S-protein/vitronectin in cell migration; **Susan Berry, M.D.**, pediatrics, \$6,500 to examine nucleotide sequence of GHRH-like substance in rat testis; **Caryl Boehner, Ph.D.**, pediatrics, \$5,000 to probe surgical outcome in death minded patients; **Arthur Caplan, Ph.D.**, center for biomedical ethics, \$6,000 for an interdisciplinary study on the ethical and policy issues involving the use of fetal tissue; **John Eaton, Ph.D.**, lab medicine and pathology, \$6,000 to investigate iron-binding substances in tobacco smoke; **Hugh Hensleigh, Ph.D.**, obstetrics and gynecology, \$3,500 to clarify the induction of sister chromatid exchange in preimplantation mouse; **Marc Jenkins, Ph.D.**, microbiology, \$10,000 to study costimulatory signals in CD4+ T cell activation; **Jonathan Parsons, Ph.D.**, cell biology and neuroanatomy, \$4,000 to analyze fluorochrome conjugated lactogen receptor probes; **Gundu Rao, Ph.D.**, lab medicine and pathology, \$12,000 for studies of phosphoinositol metabolism in platelets; **Robert Roon, Ph.D.**, biochemistry, \$5,000 to clarify L-glutamine transport in the central nervous system; **Ralph Shapiro, M.D.**, pediatrics, \$10,000 to study the genetic effects of alpha interferon on lymphocytes; **Clark Smith II, M.D.**, pediatrics, \$7,000 to determine the mechanics of megakaryocyte maturation and platelet release; and **Robert Vessella, Ph.D.**, urologic surgery, \$5,000 for a parallel processor for radiolabeled monoclonal antibody dosimetry.

Special grants include: **Stanley Erlandsen, Ph.D.**, cell biology and neuroanatomy, \$12,000 for an ion tech micro sputter coater for LVSEM; **Ashley Haase, M.D.**, microbiology, \$45,491 for a sun4/260C computer and related hardware; **David Hamilton, Ph.D.**, cell biology and neuroanatomy, \$94,000

Robert J. Roon: MMF Grant Recipient

Dr. Robert J. Roon, an associate professor of biochemistry, was one of 13 faculty members to receive a research grant at the Minnesota Medical Foundation's spring meeting of the board of trustees. In all, the MMF board approved more than \$355,000 in faculty research grants, student research grants, and special grants (see adjacent article).

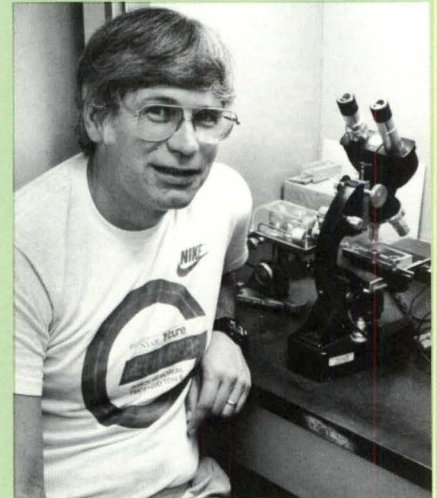
Roon received \$5,000 for a project investigating L-glutamine transport in the central nervous system. Research associates in the study are Dr. James Koerner, biochemistry, and Dr. Rodney Johnson, medicinal chemistry.

The project description reads: "The acidic amino acids including L-glutamate serve as the primary neurotransmitters in the brain, and alterations in their function may result in serious neurological disorders. We are studying the metabolic pathways by which these neurotransmitters are synthesized from L-glutamine, focusing on the transport of L-glutamine into neurons."

Of progress to date in other laboratories, Roon writes: "The kinetic data on L-glutamine transport are fragmentary and reports from various laboratories are somewhat contradictory. To date, no attempt has been made to investigate glutamine transport in purified membrane vesicles and no one has isolated transport proteins.

"During the past six months (in our laboratory) we have characterized a glutamine transport system from rat brain using purified synaptic plasma membrane vesicles. . . This study appears to be the first characterization of glutamine transport in the central nervous system which has employed purified synaptic membrane vesicles and serves as a first step toward reconstituting and purifying a glutamine transport system."

The immediate goals of the research project are to characterize the major



Dr. Robert Roon

glutamine transport systems in the central nervous system using uptake studies with purified membrane vesicles; develop methods for extracting the transport proteins from the vesicles and reconstituting transport activity in artificial proteoliposomes; and begin to purify the transport proteins using reconstitution of activity as an assay.

Future goals as stated by Roon are: purify the proteins to homogeneity and undertake partial amino acid sequencing; make poly- and monoclonal antibodies to the proteins; using specific antibody staining techniques, identify the localization of the transport systems in the central nervous system; using amino acid sequence data, construct DNA hybridization probes in order to clone the structural genes encoding the transport proteins; and determine the complete nucleotide sequence of genes encoding the transport proteins.

Roon has been a faculty member in the Department of Biochemistry since 1971. He received his Ph.D. from the University of Michigan in 1969, and is originally from Grand Rapids, Michigan. □

for a confocal laser scanning microscope; **H.P.C. Hogenkamp, Ph.D.**, biochemistry, \$45,025 for an autoclave; **Harry Orr, Ph.D.**, institute for human genetics, \$28,250 to establish a transgenic mouse facility; **John Strickler Jr., M.D.**, lab medicine and pathology, \$15,000 for in situ hybridization studies of bone marrow; and **James G. White, M.D.**, lab medicine and pathology, \$23,740 for studies on the interac-

tion of normal and abnormal platelets with damaged vascular surfaces.

Student grants include: **Annette Hanson**, \$1,200 to explore the behavioral sensitivity to a selective D2 agonist modulated by a calcium channel antagonist; **David Kendall**, \$1,200 to characterize the metabolic effect of hemipancnectomy in living related pancreas donors; glucose homeostasis and effect on secondary complications of

diabetes; **John Rogers**, \$1,200 to explore hypoxia's effect on macrophage monokine production; and **Marilyn Weber**, \$1,200 to clarify the effect of rotating insulin injection sites on glycemic control. □

MMF announces grants 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 fellowships were recently announced by MMF.

Bacaner Awards

Seven graduate students in the Medical School's basic sciences were selected to receive the Bacaner Awards. Named in memory of Jacob and Minnie Bacaner, these \$500 cash awards are given to recognize creative research in the six basic science areas. For 1988, Bacaner Award winners are: **Taowen Chung** and **Frank Rusnak, Ph.D.**, co-winners in biochemistry; **Paula Schueler**, cell biology and neuroanatomy; **Chris Con-tag**, microbiology; **Robert Haire**, laboratory medicine and pathology; **Carl Manthey**, pharmacology; and **Margaret Kruse**, physiology.

Daniel A. Coyle Award

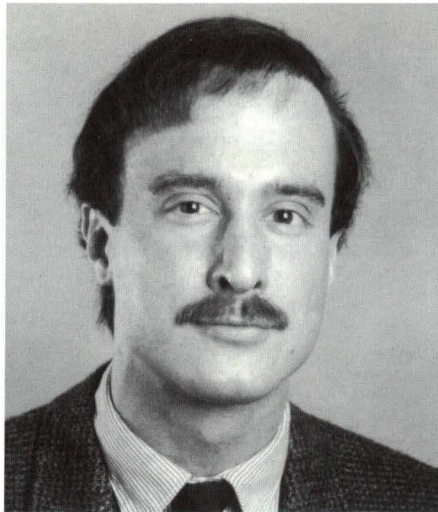
Marie Welshinger is the 1988 recipient of the Daniel A. Coyle Award. The \$100 award is given to an outstanding woman medical student in the field of obstetrics and gynecology.

Wallace D. Armstrong Award

The Wallace D. Armstrong Award for 1988 was given to **Bernard Erickson**. The \$500 award is given in memory of Dr. Armstrong, former chairman of the Department of Biochemistry, and recognizes superior achievement in biochemistry.

Gail Parker-Eady Memorial Award

Established in 1980 in memory of Dr. Eady, a graduate of the class of 1980, the Gail Parker-Eady Award is given to a student among the minority members of the senior class who has displayed high academic achievement and humanitarian spirit. The 1988 winner of the \$500 award is **Garry Walker**.



Daniel Boue

J. Jacob Kaplan Research Award

This year's \$1,500 research achievement award is presented in the field of immunology in the diagnosis and treatment of cancer to **Rod Feddersen**. Established from an endowment from the late Dr. J. Jacob Kaplan, a 1939 alumnus of the Medical School, the Kaplan award rotates annually among three medical fields: gastroenterology, cardiology, and immunology in the diagnosis and treatment of cancer.

J. Thomas Livermore Award

Daniel Boue has been named the 1988 recipient of the J. Thomas Livermore Award. This \$1,000 cash prize has been awarded since 1971 to a medical student who has accomplished outstanding original research in the field of hematology. The award is made possible by the contributions of the family of Thomas Livermore, who died of leukemia as a young adult.

Medical Student Achievement Awards

Student Achievement Awards are given to fourth-year medical students in recognition of exceptional leadership service and achievement while in medical school and promise for future contributions to the field of medicine. The 1988 recipients are **Darla Granger**, **Sarah Kaus**, **Jon Ritter**, and **Michael Swenson**. Each recipient receives a certificate and a \$1,000 cash prize. Students are nominated for the awards by faculty and other medical students with the final selection being made by MMF's Honors and Awards Committee.

Undergraduate Research Award

The Undergraduate Research Award for 1988 was given to **Joanne Hilden** for her paper entitled "DQ-beta sequences in HLA-DR4 haplotypes." The \$500 award goes to a member of the graduating class who submits what is judged to be the best student research paper.

Richard C. Horns Memorial Award

The Richard C. Horns Memorial Award is given to a senior medical student who has the ability to relate to patients, to observe and analyze data for diagnosis and treatment, and the curiosity and broad interest which lends human perspective to clinical practice. **David Kendall** is the 1988 recipient of this \$500 award. Dr. Horns, a 1943 graduate of the University of Minnesota Medical School, was a professor of ophthalmology at the University. □

Dr. French hosts California alumni

The Pauma Valley, Calif., home of Dr. Lyle French was the setting for a gathering in March of alumni and friends of the University of Minnesota Medical School. Approximately 60 guests enjoyed a buffet luncheon and good fellowship, and shared memories of the Medical School.

Dr. French, Class of 1939, is professor emeritus of the Department of Neurosurgery and former vice president for Health Sciences. His career at the University spanned 35 years. At Dr. French's retirement in 1982 as vice president of Health Sciences, the Lyle A. French Chair in Neurosurgery was established in his honor.



David Teslow, MMF executive director, presents a special donor plaque to **Joseph Dasset, M.D., '26**, at the Lyle French reception.

Dr. French and his wife, Gene, continue to actively support the University of Minnesota Medical School. □

ALUMNI UPDATE

Dear Colleagues:

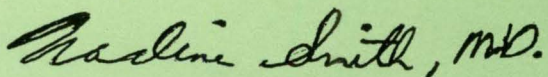
Another alumni program year has come to an end and I am delighted to say that it has been a successful one. This year's "Alumni Weekend" featured reunions for the Medical School classes of 1938, 1948, 1958, 1963, 1968, and 1978, and included a special program for the Class of 1988 as well as the New Horizons in Minnesota Medicine seminar. We also held our first Medical Alumni Reunion Golf Tournament, and the Twin Cities alumni of 1937 and earlier started a Half Century Club. I thank all of you who helped make these events possible.

The coming year is a very special one for the Medical School. From September through June of 1989, the University of Minnesota Medical School celebrates its 100th anniversary. The Minnesota Medical Foundation (established at the Medical School's 50th anniversary) will celebrate its 50th anniversary. Many events, speakers, displays, and other happenings are scheduled to commemorate this occasion. Please join me in showing our pride in the Medical School by participating in the anniversary celebration. (Watch for more details in the fall issue.)

The Medical Alumni Society's annual meeting last month brought us new board members and officers. I am pleased to announce that Dr. Frank Lushine, '71, will be serving as the 1988-89 president of the Medical Alumni Society. I am confident that Dr. Lushine will successfully guide us through the anniversary year, and I wish him and his board members much success.

Once again, I thank you for your support during this past year. Please help me in welcoming the Class of 1988 into the ranks of alumni and wishing them long and fulfilling careers in the field of medicine.

Sincerely,



Nadine G. Smith, M.D., '52
President
Medical Alumni Society

P.S. Keep sending in those professional updates. For many of us, the "Class Notes" section of the *Medical Bulletin* is the only source of information about some of our colleagues.

Diehl Award Winners

Chester A. Anderson, M.D., Class of 1944; Robert B. Howard, M.D., Class of 1944; and Arnold J. Kremen, M.D., Class of 1937, were selected to receive the 1988 Harold S. Diehl Award presented by the Minnesota Alumni Society at its annual luncheon meeting on June 4. The Diehl Award is given to recognize alumni of the University of Minnesota Medical School who have made outstanding contributions to the school, the University, and the community.

Chester A. Anderson

Dr. Chester A. Anderson operated a solo family practice in Hector, Minnesota (population 1,300) from 1948 until he retired in 1985. Despite this busy practice, Dr. Anderson found time to actively participate in a multitude of activities to promote organized medicine. He worked for the establishment of a Department of Family Practice at the University of Minnesota, and he was an active medical issue lobbyist at the State Legislature for many years.

Through the years, Dr. Anderson has taken great interest in the activities of the Minnesota Academy of Family Physicians and the Minnesota Medical Association. He has served in many capacities for both organizations including holding office as president of each.

Dr. Anderson has been honored with numerous awards in recognition of his many contributions to medicine. He received the Good Housekeeping Award as one of the ten outstanding family practitioners in the country in 1981, the National Family Doctor of the Year Award from the American Academy of Family Physicians in 1983, the Minnesota Academy of Family Physicians Merit Award in 1974, the Minnesota Family Doctor of the Year Award in 1983, and the Minnesota Medical Association's Distinguished Service Award in 1978.

Robert B. Howard

Dr. Robert B. Howard joined the faculty of the University of Minnesota in 1948 as a teaching fellow in internal medicine. He rose through the ranks and was appointed full professor in 1958. During this time, he also served as director of the Continuing Medical Education Department.

In 1958, he was appointed dean of the Medical School, a position he held for the next 12 years. When he resigned as

dean, Dr. Howard renewed his interest in hematology and spent the next year at the Gastarzt in Medizin in Zurich.

In 1983, Dr. Howard turned to editing and has served as editor-and-chief of *Postgraduate Medicine* ever since. He is credited with turning the magazine into a significant instrument of continuing medical education for primary care physicians throughout the country.

Dr. Howard has also been active in professional and community organizations. He has served on several committees for the National Institutes of Health, on the Surgeon General's Advisory Committee on Indian Health, on the Governor's Advisory Council on Health, Welfare, and Rehabilitation, on Hamline University's board of trustees, on the board of Walker Methodist Residence, and on various committees of the county and state medical societies.

Arnold J. Kremen

A noted leader in the fields of abdominal and head and neck surgery, Dr. Arnold J. Kremen has had a distinguished career as surgeon and educator.

For many years, he was active academically in the University of Minnesota's Department of Surgery, beginning as an instructor in 1947. He left in 1954 as an associate professor to become a professor of clinical surgery at Columbia University College of Physicians and Surgeons in New York. When he returned to Minneapolis to take up private practice,



Diehl Award winners Arnold Kremen, Robert Howard, and Chester Anderson.

he also returned to the University of Minnesota as a clinical professor of surgery, a position he holds to date. Dr. Kremen has also been active in the training and education of surgical residents at Mount Sinai Hospital in Minneapolis.

In addition to his private practice and his educational duties, Dr. Kremen participates in several professional organizations including the American Medical Association, the Minnesota Medical Association, the Hennepin County Medical Society, the Society of University Surgeons, the American Surgical Association, the Society of Head and Neck Surgeons, the Societe Internationale de Chirurgie, and the Cancer Commission of American College Surgeons. He has also served on the board of trustees of the Minnesota Medical Foundation.

PAST RECIPIENTS

1962 Owen Wangenstein	1973 Phillip Halenbeck	1980 Helen L. Knudsen
1963 Donald J. Cowling	Olga Hansen	Donald Stewart
Charles G. Sheppard	Litzenberg	1981 Eva Jane (Ostegren)
1964 Vernon D.E. Smith	1974 Ann Arnold	Larson
1965 Karl W. Anderson	Roger MacDonald	Carl Ragnar Wall
1966 J. Arthur Myers	Carl O. Rice	1982 Stuart Lane Arey
1967 Theodore Fritsche	R.S. Ylvisaker	Kristofer Hagen
1968 Walter Halloran	1975 Reuben Berman	1983 John J. Regan Sr.
Anderson C. Hilding	Bror Pearson	John J. Eustermann
Carl Holmstrom	Lawrence Richdorff	1984 Arnold S. Anderson
1969 Karl R. Lundeberg	1976 Milton Hurwitz	John W. Anderson
1970 Robert Barr	Leonard Lang	1985 Kenneth W. Covey
LeRoy Larson	Russell Sather	Frank E. Johnson
1971 William C. Bernstein	1977 Virgil J.P. Lundquist	1986 A. Boyd Thomes
J.C. Grant	Ruth Boynton	1987 Malcolm E. Fifield
1972 J. Richards Aurelius	1978 Herman Drill	Marcy L. Ditmanson
Reino Puumala	Lester Bendix	
Marie Bepko Puumala	1979 Miland Knapp	
Ricard Puumala	Harold Wilmot	
Barbara Puumala		

Alumni Reunions: A Celebration...

Spirits were high as University of Minnesota Medical School graduates from the classes of 1938, 1948, 1958, 1963, 1968, and 1978 arrived on campus the first weekend in June. Numerous activities were planned, but there was still plenty of time for class members to renew old friendships and reminisce about their days in medical school.

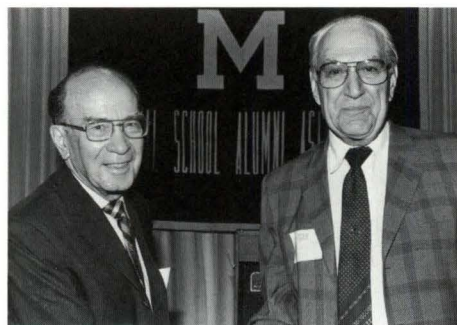
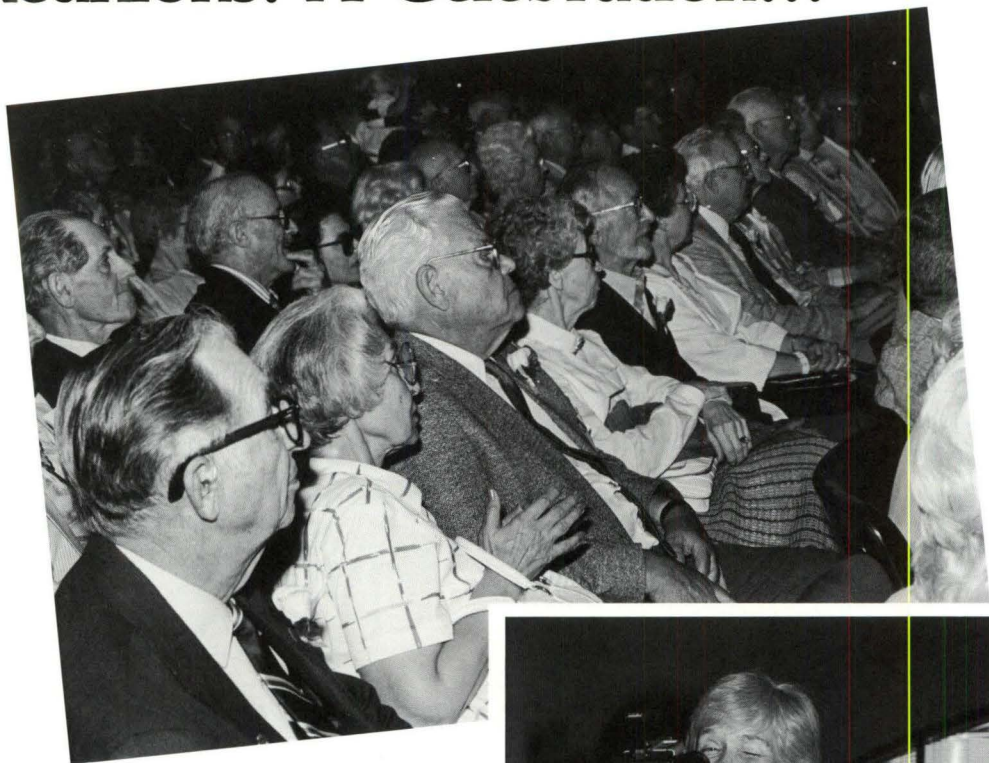
The 50th Reunion Class kicked off the weekend on Thursday with a tour of the new University of Minnesota Hospital. An evening social hour at the Radisson University Hotel, headquarters for the three-day event, was spent greeting returning classmates.

Friday was a full day, beginning with the first-ever Half Century Club Reunion for alumni who graduated from medical school more than 50 years ago. Members of the Class of 1938 and the Half Century Club were welcomed at a luncheon in their honor by Dean David Brown, who updated them on the exciting progress the Medical School is making in education and research. In the afternoon, graduates from 1938 were special guests at the commencement ceremony for the Class of 1988 in Northrop Auditorium.

A new event this year was a golf tournament at the Les Bolstad Golf Course for the classes of 1963, 1968, and 1978. Eager participants enjoyed warm sun and good fellowship in an event that promises to become a popular annual function.

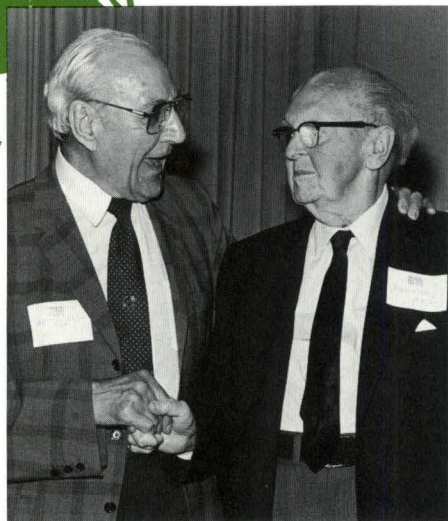
The evening was reserved for the All Alumni Reception at the Radisson University Hotel, followed by individual banquets and programs scheduled for each reunion class. The festive decor and an enthusiastic band added to the enjoyment of the approximately 400 alumni and guests participating in the celebration.

The reunion weekend concluded on Saturday with New Horizons in Minnesota Medicine, a continuing medical education seminar featuring six faculty members of the University of Minnesota Medical School. The faculty speakers, all leaders in their respective areas, detailed the innovative research taking place at the Medical School.





...Half Century Club Reunion



Dr. Herman (Tiny) Drill greets Dr. Royal Gray at the Half Century Club Reunion.

University of Minnesota Medical School alumni from 1937 or earlier gathered June 3 to participate in the first-ever Half Century Club Reunion. Created for Twin Cities graduates who have already celebrated their 50th reunion, the Half Century Club provides ongoing fellowship to older medical alumni.

Leonard Wilson, Ph.D., professor in the Department of History of Medicine, highlighted the Medical School's history from 1914 to 1937 and answered participants' questions. Afterwards, all attendees were officially inducted into the Half Century Club by chairperson Herman "Tiny" Drill, M.D., '28.

Plans call for the Half Century Club Reunion to expand next year as part of the 100th Anniversary Celebration. All alumni from 1938 or earlier will be invited to visit the campus and participate in the festivities. Questions about Half Century Club activities can be directed to Bob Burgett at the Minnesota Medical Foundation Alumni Office, (612) 625-0972.



This year's inaugural University of Minnesota Medical School Golf Tournament was one of the most enjoyed reunion events. Suggested by 1968 reunion chairperson, Dr. Jack Dunne, the tournament was played at the University's Les Bolstad Golf Course and featured entrants from the classes of 1963, 1968, and 1978. Plans are to expand the tournament next year and make it an annual part of Reunion Weekend. This year's winners were: 1st Place, Dr. John Mahler, '63 (76); 2nd Place, Dr. Mike Magnusson, '68 (82); and Blind Bogey, Dr. John Mahler, '63 (62).

Pictured above from the Class of 1968 are: Jack Dunne, John Zurek, Bob Wright, and Mark Dahl.

...First Reunion: Class of 1988

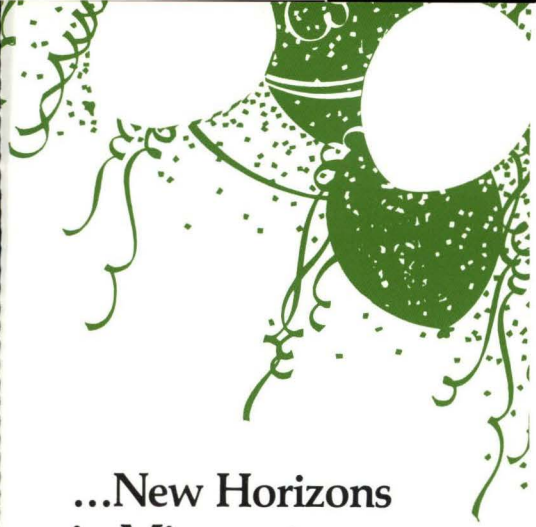
The First Reunion Celebration of the University of Minnesota Medical School Class of 1988 was held June 1 at the International Market Square Atrium in Minneapolis. Organized by class members, the event was sponsored by the Medical Student Notetaking Cooperative, the Medical Alumni Society, and the Minnesota Medical Foundation.

A slide show presentation combined with socializing, dancing, and food provided a comfortable atmosphere where classmates could reminisce and share four years worth of medical school stories.

Representatives of the Minnesota Medical Foundation, the Minnesota Alumni Association, the Medical Alumni Society, and fellow class members offered wishes for success and fulfillment to the Class of 1988 throughout their careers in medicine.



Members of the Class of 1988 celebrate their first reunion.



Residents Away From Home

...New Horizons in Minnesota Medicine

A memorable part of the reunion weekend was the New Horizons in Minnesota Medicine seminar, held on Saturday, June 4. The seminar is an annual presentation of the Medical Alumni Society featuring six faculty members of the University of Minnesota Medical School.

Scheduled in conjunction with Medical School graduation ceremonies and class reunion activities, New Horizons offers an opportunity to both local and visiting alumni to learn about new technologies and the exciting research being conducted at the University of Minnesota.

Speakers this year included Dr. Frank Rhame, assistant professor, Infectious Disease Section, Department of Medicine, speaking on "AIDS Research in Minnesota," Dr. Louis Tobian Jr., professor of medicine, speaking on "Protection by Dietary Potassium Against Hypertensive Stroke Deaths, Kidney Disease, Endothelial Cell Injury: A Legacy from Prehistoric Times," Dr. Norma K.C. Ramsay, professor of pediatrics and director, Pediatric Bone Marrow Transplantation Unit, speaking on "Improved Survival for Children with Cancer," Dr. John Delaney, professor of surgery, speaking on "Treatment of Cancer with Breast Preservation," Dr. Donald Doughman, professor and chairman, Department of Ophthalmology, speaking on "Ophthalmology 1988: An Update," and Dr. Robert Kane, professor and dean, School of Public Health, speaking on "Caring for Older Patients: Facing Tough Decisions."

In their continuing effort to find ways of enhancing the "student experience" at the Medical Schools, the Medical Alumni Society board of directors last fall voted to revive a once popular program—Residents Away From Home.

The Residents Away From Home (RAFH) program is designed to facilitate the medical student's residency search by putting the student in contact with a volunteer Medical School alumnus in the target city. As RAFH committee co-chair Margaret Macrae explains, "This alumnus can be a very helpful source of inside information on matters ranging from the strengths and weaknesses of a particular residency program to the general quality of life in that area of the country. This vital information is often difficult to come by through other means."

In some instances alumni might even provide students with overnight accommodations in their homes. This can be

especially helpful in defraying the total cost of the residency search, which amounts to well over \$1,000 for most students.

"This is a great program and a great way for alumni to keep in touch with our future colleagues," committee co-chair Celeste Madrid Taylor remarks. "I hope all alumni will take advantage of this wonderful opportunity. Alumni in major metropolitan areas outside Minnesota are especially needed. We plan to have the program up and running for this next year's search."

Please complete the response card below if you are willing to participate as an alumni contact person. Be sure to indicate whether or not you are able to host a student overnight. Then send the card to the address shown no later than September 30, 1988.

Your helpfulness will be greatly appreciated.

RESIDENTS AWAY FROM HOME

Alumni Volunteer Form

Yes, I want to help medical students with their residency search.

Yes, I can host a student overnight.

No, I cannot host a student overnight, but I am willing to answer student questions about a residency site in my area.

NAME _____ CLASS YEAR _____

ADDRESS _____

CITY, STATE, ZIP _____

DAYTIME PHONE () _____ EVENING () _____

My own residency was at: _____

My area of specialty is: _____

MAIL TO: RESIDENTS AWAY FROM HOME
Box 193, UMHC
University of Minnesota Medical School
Minneapolis, MN 55455

MAS BOARD NEWS

Medical Alumni Society elections

New officers and board members were nominated at the May 10 meeting of the MAS board of directors. All nominations were accepted and passed to the entire society for election at the June 4 annual meeting.

The 1988-89 Medical Alumni Society board of directors is:

Officers:

- *President - Frank Lushine, M.D., '71
- Vice President - Richard Student, M.D., '54
- Secretary/Treasurer - Margaret Macrae, M.D., '74
- Past President - Nadine Smith, M.D., '52

Directors:

- John W. Anderson, M.D., '51
- Ken Berge, M.D., '51
- Gary Falk, M.D., '68
- *N.L. Gault Jr., M.D., '50
- Roy Good, M.D., '52

*Re-elected to three-year term

**Newly elected to three-year term

- Dorothy Horns, M.D., '76
- John O'Leary, M.D., '77
- **Elmer Paulson, M.D., '37
- **Richard Simmons, M.D., '55
- *Donald Swenson, M.D., '51
- George Tani, M.D., '50
- Celeste Madrid Taylor, M.D., '84

Ex-officio members

- David Brown, M.D. - Dean of the Twin Cities Medical School
- H. Mead Cavert, M.D., '50 - Associate Dean
- Konald Prem, M.D. - Faculty Advisor
- David Teslow - Executive Director, Minnesota Medical Foundation
- Margaret Carlson - Executive Director, Minnesota Alumni Association
- Jeff Klensz - Medical Student Council
- Robert Burgett - Minnesota Medical Foundation
- Mark Holman - Minnesota Medical Foundation

CLASS NOTES

1932

Dr. Clayton T. Beecham, Sunbury, Pennsylvania, has been presented with the Distinguished Service Award by the American College of Obstetricians and Gynecologists "in recognition and appreciation of outstanding contributions to the discipline of gynecology and obstetrics." These include: professor and director of gynecologic oncology, Temple University Hospital; director of gynecology-obstetrics, Geisinger Medical Center; president of the American Association of Obstetricians and Gynecologists; and examiner for the American Board of Obstetrics and Gynecology.

1937

Dr. Robert B. Tudor, a Bismarck, North Dakota, pediatrician who has practiced medicine for more than 50 years, has been awarded the 1988 Physician Professional and Community Service Award by the North Dakota Medical Association. It is the association's highest honor. Dr. Tudor has served in a number of professional organizations, and has authored more than 100 articles. In 1959, he founded the national Childhood Gastroenterology Registry, and 20 years later founded the Bismarck-Mandan Rape Victims Advocacy Program. A sports enthusiast, Dr. Tudor has served as attending physician for the U.S. Wrestling Team and for the U.S. Olympic Training Center at Squaw Valley.

1938

Dr. Milan Novak, Tucson, Arizona, still active at age 80, is chairman of the Human Subjects Committee and lecturer in the College of Medicine at the University of Arizona. The committee has the authority to prevent any research project from being established if it appears it may violate civil rights or compromise the welfare of volunteers. Dr. Novak's wife, Dorothy, is active as a lay community advisor at the University Medical Center.



MAS officers and board members include (seated) Dorothy Horns, M.D., '76; Nadine Smith, M.D., '52; Don Swenson, M.D., '51; (standing) Mark Holman, MMF; George Tani, M.D., '51; Frank Lushine, M.D., '71; Celeste Madrid Taylor, M.D., '84; Margaret Macrae, M.D., '74; Richard Student, M.D., '54; Roy Good, M.D., '52; Mead Cavert, M.D., '50; Bob Burgett and David Teslow, MMF.

1947

Dr. John R. Watson, Medford, Oregon, is currently chairman of the Mayo Alumni Association of Oregon. He is coordinating a summer meeting and banquet to be held concurrently with the regional Shakespearean Festival and Classical Music Festival.

1956

Dr. Stanley M. Goldberg, Minneapolis, was the Moynihan Lecturer at the meeting of the Association of Surgeons of Great Britain and Ireland in Harrogate, England, in April. He was also a visiting professor to the University of Bristol and the University of Wales, as well as Yale University, in April.

1960

Dr. Vincent R. Hunt, Pawtucket, Rhode Island, assumed the chairmanship of the Department of Family Medicine at Brown University and was named physician-in-chief, Department of Family Medicine, Memorial Hospital of Rhode Island in 1986, and was recently appointed Frederick Henry Prince Distinguished Scholar in Family Medicine upon recommendation of the Academic Council of Brown University. Dr. Hunt was director of the Family Medicine Residency at St. Paul Ramsey Medical Center from 1970 to 1985. He has served as consultant to family medicine programs around the world in such countries as Korea, Lebanon, Costa Rica, and Nicaragua.

1961

Dr. Bruce Bart, chief of dermatology at Hennepin County Medical Center since 1970, became a full-time member of the faculty on July 1, 1988. He has been in private practice with Dr. Alvin Zelickson (Class of 1955) in Minneapolis and Wayzata. Dr. Bart is clinical professor of dermatology on the faculty of the University of Minnesota Medical School.

1975

Dr. Donald A. Baker, Spokane, Washington, was recently awarded a patent

for the world's first automatic, non-invasive ambulatory fetal monitor capable of continuous fetal non-stress testing. The attached, battery operated, programmable mini-computer compares the tested fetal heart movement data to accepted norms in order to increase the obstetrician's surveillance time to identify and prevent factors contributing to in-utero fetal hypoxic-neurologic injury.

1981

Dr. Barbara L. Pohlman, Laguna Niguel, California, began full-time employment with Pacific Bell in November 1987 and became medical director for Southern California in January 1988. Dr. Pohlman continues as assistant clinical professor of medicine at the University of California, Irvine, Southern Occupational Health Center.

Alumni Directories coming

The 1988 Centennial Edition of the University of Minnesota Medical School Alumni Directory will be available this coming fall.

The Alumni Directory is a valuable resource for renewing acquaintances with classmates and locating professional colleagues. Names, addresses, and specialties of the Medical School alumni are included, along with listings by geographical area and class year.

Details on acquiring an Alumni Directory will be included in the Fall 1988 *Medical Bulletin*. Information will also be provided during the Fall Alumni Phonathon.

What's New With You?

Name Specialty/Degree Year

Address Telephone

City, State, Zip

News of relocations, new positions, honors and awards, community activities, personal activities, etc.

Send to: Editor, Minnesota Medical Foundation, Box 193 UMHC,
University of Minnesota, Minneapolis, MN 55455.

IN MEMORIAM

Lloyd G. Edwards, M.D.,

Class of 1943, died April 17 at age 70. A resident of Mendota Heights, Minnesota, Dr. Edwards was in practice as an eye, ear, nose, and throat specialist from the mid-1940s until his retirement in 1983. He served two years in the Army medical corps in World War II after finishing his internship in 1943, reaching the rank of major. Dr. Edwards is survived by his wife, Audrey, two sons, three daughters, four brothers, a sister, and 14 grandchildren.

Marian Grimes, M.D.,

Class of 1927, died April 22 at age 85. One of Minneapolis' pioneer female physicians, Dr. Grimes maintained a private practice in obstetrics and gynecology and was on the staff of St. Barnabas Hospital for 38 years before retiring in 1968. She served another 15 years after retirement as a volunteer gynecologist at the University of Minnesota's Cancer Detection Center. Dr. Grimes did post-graduate work at the New York Academy of Medicine and studied for a year in Vienna. She was made a diplomate of the National Board of Medical Examiners in 1931. Dr. Grimes is survived by a sister-in-law, two nephews, five nieces, and five grand-nieces and nephews.

Everett Hanson, M.D.,

Class of 1927, died February 29 at age 88. Dr. Hanson was a general practitioner in New York Mills, Minnesota, for 44 years. He was a member of the New York Mills school board, and was on the staff of Tri-County Hospital in Wadena, St. James Hospital in Perham, and New York Mills Community Hospital. Dr. Hanson was a 50-year member of the Minnesota Medical Association. In 1980 he was named state VFW Outstanding Citizen of the Year for his community service. Dr. Hanson is survived by his wife, Myrtle, and a daughter.

Solomon E. Howard, M.D.,

Class of 1929, died April 22 at age 85. Dr. Howard was born in Romania and came to this country in 1905, later working as a high school teacher and coach to raise money for medical school. At age 40, he enlisted in the Army and served as a physician in North Africa and France for three years. Dr. Howard practiced

dermatology in downtown Minneapolis for 50 years, and after retirement spent his time working with his three major hobbies: photography, gardening, and history. Memorials to the Minnesota Medical Foundation were suggested. Dr. Howard is survived by his wife, Sylvia, two sons, three daughters, two sisters, and five grandchildren.

Herman M. Juergens, M.D.,

Class of 1920, died May 9 at age 93. Dr. Juergens practiced medicine in Belle Plaine, Minnesota, for 46 years, and also served as Scott County coroner. In 1972, he was selected as the outstanding senior citizen of Scott County. Dr. Juergens is survived by his wife, Leona, a son, a daughter, 11 grandchildren, and 16 great-grandchildren.

Frank J. Kucera, M.D.,

Class of 1921, died April 21 at age 93. Dr. Kucera was a family physician in Hopkins, Minnesota, for 55 years. He was active in community events, and was an instigator of the first immunization program in area schools. Dr. Kucera is survived by his wife, Alma, a daughter, two sons, a brother, six grandchildren, and one great-grandchild.

George H. Marking, M.D.,

Class of 1936, died March 22 at age 77. Dr. Marking was a practicing physician in Minneapolis for 52 years, specializing in family practice. He was associated with the Metropolitan Medical Center, and was an active member of the Sons of Norway Lodge. He is survived by his wife, Jeanette, two daughters, a son, and six grandchildren.

John J. Marren, M.D.,

Class of 1930, died February 12 in Napa, California, at age 83. A native of Two Harbors, Minnesota, Dr. Marren served in the Pacific during World War II, and retired as a full medical colonel. He became an American Board of Neurology and Psychiatry Diplomate in 1950, and was a Fellow of the American Psychiatric Association. After moving to Napa in 1960, Dr. Marren became chief of neurology at the California Veterans Home in Yountville, California. He is survived by his wife, Lucille, a daughter, a son, and five grandchildren.

Harvey C. Maxwell, M.D.,

Class of 1925, died February 24. A resident of Laguna Beach, California, Dr. Maxwell was a retired colonel with the Army Medical Corps. He also was an internationally known lawn bowler and was author of "Maxwell's Lawn Bowling Guide."

Osler L. Peterson, M.D.,

Class of 1938, died January 17 at age 75. Dr. Peterson was a retired Harvard Medical School professor and an internationally known pioneer in health services research. He joined the Virus Laboratory at the Rockefeller Institute in 1943 and served as a Rockefeller Foundation staff member from 1944 to 1956. Dr. Peterson joined the Harvard Medical School faculty in 1959 and established a teaching and research program in social medicine for undergraduate medical students. He was appointed professor of preventive medicine in 1968, a post he held until retirement from Harvard in 1977, when he became research professor at the University of Pennsylvania Medical School. Dr. Peterson is survived by his wife, Delores, and two sons.

Robert G. Rossing, M.D.,

Class of 1948, died March 9 at age 62. A resident of Temple, Texas, Dr. Rossing served as a medical officer in the Korean War and was on the faculty of the University of Minnesota Medical School. He was a research physician at the School of Aerospace Medicine in San Antonio, and was associate chief of staff for research and for education at the Teague Veterans Hospital in Temple. Dr. Rossing also was a faculty member of Texas A & M Medical School. He is survived by his wife, Nona, three sons, and four grandchildren.

Thomas T. Semba, M.D.,

Class of 1951, died May 2 at age 64. Dr. Semba was chief pathologist at North Memorial Medical Center in Robbinsdale, Minnesota, and guided the growth of the Pathology Department at North Memorial from 1960 to the present. He also taught laboratory medicine and pathology at the University of Minnesota Medical School for the past 16 years. Dr. Semba is survived by his wife, Hannah, and four children, all of whom are physicians.

David McQuarrie Worthen, M.D.,

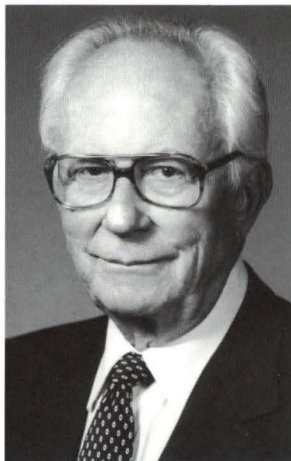
Class of 1961, died April 14 at age 51. A Veterans Administration ophthalmologist, Dr. Worthen was the VA's assistant chief medical director for academic affairs and a member of the medical school faculties of Georgetown, Howard, and Johns Hopkins universities. He also had served on 17 advisory groups on medical education, government regulation, health, and fitness. At his retirement for medical disability, the VA established a David M. Worthen Award for academic excellence, and the American Medical Association voted him a special commendation for his "great character and courage" and his contributions to medical education and eye care. Dr. Worthen's story of living with amyotrophic lateral sclerosis (Lou Gehrig's disease) was published in the *Journal of the American Medical Association* and *The Washington Post*. Dr. Worthen is survived by his wife, Gaye, three sons, two daughters, two brothers, and a sister.

We have also received notice of the deaths of the following non-alumni physicians:

John Howard Moe, M.D.,

Professor Emeritus of the Medical School's Department of Orthopaedic Surgery, died April 2 at age 82. Dr. Moe was a pioneer in the treatment of scoliosis, and his contributions to the field of orthopaedic surgery during his 50-year career are many.

In 1948, he established a scoliosis service at Gillette Children's Hospital, dedicated to finding new techniques for managing children crippled with spinal deformities. He founded the Scoliosis Research Society in 1966 and served as its first president. In the 1970s he established the Twin Cities Scoliosis Center as part of the University of Minnesota's Department of Orthopaedic Surgery. Under his direction, the center treated more than 20,000 patients, trained physicians from around the world in managing spinal diseases, and sponsored research of innovative treatment methods. Dr. Moe was also past president of the American Orthopaedic Association, recipient of the Charles Bolles-Bolles Rogers Award of the Hennepin County Medical Society, and held numerous



Dr. John H. Moe



Dr. Frederick E. Shideman



Dr. Wesley W. Spink

other national and international memberships and awards.

Memorials have been directed to the John H. Moe Scoliosis Fund, administered by the Minnesota Medical Foundation, which has been established to provide support for research and education into this disease. Dr. Moe is survived by his wife, Mary Lou, a son, a daughter, four step-children, and 17 grandchildren.

Frederick E. Shideman, M.D.,

Former professor and head of the Pharmacology Department at the University of Minnesota Medical School, died April 21 at age 72. Dr. Shideman joined the Medical School faculty in 1962 after 10 years at the University of Wisconsin, and was instrumental in the remarkable growth of the department during his 25 years as chairman.

Dr. Shideman was active in sponsoring South Korean physicians and students to come and study at the University of Minnesota Department of Pharmacology, and received an honorary degree from Yonsei University in Seoul for helping reorganize its Pharmacology Department. In 1961 he was appointed a Fellow in the Royal Society of Medicine, an English medical society, and in 1965 was made an honorary member of the Korean Medical Association.

The Department of Pharmacology at the University of Minnesota, through the Minnesota Medical Foundation, has established the Frederick E. Shideman Fund, with the objective of using the investment income to support research and training in pharmacology. The Frederick E. Shideman-Sterling Drug Visiting

Professor Program, which promotes the interchange of knowledge between colleges and universities in the field of pharmacology, also attests to Dr. Shideman's vital role in the department. He is survived by his wife, Margaret, two sons, two daughters, and 11 grandchildren.

Wesley W. Spink, M.D.,

University of Minnesota regents' professor emeritus of medicine and comparative medicine, died May 14 at age 83. Dr. Spink was an international authority on infectious diseases and brucellosis. He conducted pioneering research on the use of sulfa drugs for therapy and administered the first penicillin and tetracycline drugs at the University of Minnesota Hospitals.

Through the efforts of Dr. Spink and his colleagues, the Minnesota Legislature in 1950 enacted a law requiring that all milk for human consumption be pasteurized. He was a brucellosis consultant to the World Health Organization and received many honors for his work.

Dr. Spink received his M.D. degree from Harvard Medical School in 1932, and joined the faculty of the University of Minnesota Medical School in 1937. In 1967 he became the first regents' professor of medicine, the highest faculty honor at the University, and in 1970 became the first professor of comparative medicine. Dr. Spink was president of the Minnesota Medical Foundation from 1954 to 1958. Memorials have been directed to the Wesley W. Spink Lectures on Comparative Medicine Fund, which is held by MMF. Dr. Spink is survived by his wife, Elizabeth, a daughter, a son, and two grandchildren.



Dr. Reuben Berman

Dear Colleagues and Friends,

This coming year we will celebrate the 100th anniversary of the founding of the University of Minnesota Medical School. Compared to the venerable schools of Europe, ours is a lusty infant. It is still possible for members of a class such as mine (1933) to know personally some alumni of every class of the Medical School's existence.

I vividly recall one member of the fifth or sixth class, Charles Erdman, who introduced us in 1928 to the anatomy of the bones. What a treat it was for us freshman that year to also watch Clarence Jackson exquisitely expose the anatomy of the tendons, nerves, and vessels of the hand. And across this 60-year span, I can still see Richard Scammon drawing on the blackboard in colored chalk — with both hands flying — creating his masterpieces of embryology.

In the short span of its existence, our Medical School has achieved worldwide acclaim. Every graduate, every student, every citizen of the state can take pride in this leadership in the medical firmament.

Now, at the start of the Medical School's second century, we have the opportunity to support our school and to demonstrate our gratitude for its role in our professional careers.

I am pleased to announce . . .

THE CENTENNIAL LAUREATE PROGRAM

to celebrate this most significant anniversary of the Medical School and the 50th anniversary of the Minnesota Medical Foundation.

The Centennial Laureate program is a way to recognize persons who make a planned gift commitment to the Medical School through the foundation. This commitment can be a gift by will, trust, or charitable life income contract. Gifts of \$10,000 or more can be used to establish named endowment funds.

Isabel and I have used a Gift Annuity, one of the charitable plans that returns a life income, to make our commitment. We hope others will want to make a planned gift commitment as well.

Reuben Berman, M.D.
Class of '33
President, Minnesota Medical Foundation, 1978-80

Dear Reuben,
I agree, our Medical School is deserving of the support of graduates and friends. I would be willing to consider becoming a part of this special Centennial Laureate Program. Please have a member of the Minnesota Medical Foundation provide additional information to me.

NAME _____

ADDRESS _____

CITY, STATE, ZIP _____ PHONE _____

Please return to: Dr. Reuben Berman
Minnesota Medical Foundation
Box 193, UMHC, Minneapolis, Minnesota 55455

HISTORICAL PERSPECTIVE

The Fourth Dean: Elias Potter Lyon (1867-1937)



Elias Potter Lyon

By Leonard G. Wilson, Ph.D.

Dean Lyon's career at Minnesota was marked by sharp contrasts and curious paradoxes. Not himself a physician, Lyon laid the foundations for the great clinical development of the Medical School. He oversaw the fourfold expansion of the University Hospital, appointed full-time chiefs of the major clinical departments, and fostered the development of great clinical teachers.

Yet the harvest of his work came late. The first half of his deanship was marked by turmoil and stagnation. Many faculty members left, not a building was built, and controversy followed controversy. Each succeeding president of the University received demands for Lyon's dismissal, but each refused. Patient, honest, imperturbable, Lyon survived successive battles to gain the respect even of his enemies and the fierce loyalty of his friends.

In the summer of 1913, at the age of 46, Lyon came from St. Louis to Minnesota, where he found himself dean of a medical faculty divided and embittered

by the reorganization of the previous winter. A year later the Medical School became embroiled in the Mayo affiliation controversy, which in 1915 caused six members of the Department of Medicine to resign in protest. In 1917 the Mayo controversy erupted again, only to be overshadowed by the outbreak of World War I. Following the war, controversy broke out again in 1921.

In 1925 Lyon began to see the first fruits of his work in the opening of the Todd and Christian wings of the University Hospital, followed in 1929 by the opening of the Eustis Children's Hospital and a new students' health service and outpatient department. Also in 1925 he was able to appoint a full-time chief of medicine, the brilliant but irascible Hilding Berglund. Two years later he appointed Leo Rigler in radiology, and sent Owen Wangenstein to Europe for a year to prepare him to take over the Department of Surgery in 1930. The same year Lyon appointed Irvine McQuarrie as chief of pediatrics.

During the 1930s, with an innovative group of young full-time chiefs of clinical departments, together with equally distinguished investigators in the medical sciences — men such as E.T. Bell, E. Allen Boyden, Hal Downey, Jesse McClendon, and A.T. Rasmussen — Minnesota began to recover the position among American medical schools that it had lost after 1913. Lyon's achievement in fostering such an unusual union of clinical and scientific investigators arose from a simple, almost naive, vision of the unity of medicine, to which he held stubbornly.

In 1916, realizing that as a physiologist by training he knew nothing of clinical medicine, and therefore of what medical students must encounter in their clinical studies, Lyon spent several days following a clinician in his work. He reported:

" . . . I saw him percuss and auscultate; I saw him count corpuscles and analyze excreta; I saw him elicit reflexes and measure temperature; I heard him speak of valves and pressure and enzymes and neurons and calories. I said 'That man is not practicing medicine. He is practicing physiology.' I watched a therapist at the bedside and found that he was not practicing medicine but pharmacology. I saw a surgeon earning a thousand dollars. I saw that he was not practicing surgery but anatomy, pathology, physiology — high finance! Finally, the relation I was seeking came suddenly into mental view. Anatomy, physiology, pharmacology, bacteriology, chemistry and the rest are not children of medicine; they are not branches of an evolutionary tree; they are not handmaids; they are not stepping stones or preparatory stages. They are it. They are medicine itself."¹

Through all the troubles and frustrations of Lyon's deanship — and they were many — that vision guided him in the development of the Medical School.

1. E.P. Lyon, "The relation of laboratory courses to the work of the clinical years," *J. Am. Med. Assoc.*, 1916, 66, 629-631.



Minnesota Medical Foundation

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August 25-27

Laser Surgery in Otolaryngology and Pulmonary Medicine

3-110 Moos Tower, University of Minnesota, Minneapolis
CME (612) 626-5525

August 26-27 (tentative)

Radiology/88

Wiley Hall, University of Minnesota, Minneapolis
CME (612) 221-3992

September 13-16

Annual Autumn Seminar on Obstetrics and Gynecology

Radisson South Hotel, Minneapolis
CME (612) 626-5525

September 14-16

Principles of Colon and Rectal Surgery

Mayo Auditorium, University of Minnesota, Minneapolis
CME (612) 626-5525

September 14-16

Obstetrics and Gynecology Annual Seminar

Radisson South Hotel, Minneapolis
CME (612) 626-5525

September 14-16

Hospital Nutrition Support

3-110 Moos Tower, University of Minnesota, Minneapolis
CME (612) 626-5525

September 15-16

Sexual Compulsivity Conference

Radisson University Hotel, Minneapolis
CME (612) 626-5525

September 19-20

Ethics Upper Limit: Health Care Resources in the '90s

Earle Brown Center, St. Paul
CME (612) 221-3992

September 30

Guilt: Recognition, Understanding, Letting Go

Earle Brown Center, St. Paul
CME (612) 221-3992

September 30

Kidney Stone Conference

Radisson University Hotel, Minneapolis (tentative)
(CME) (612) 626-5525

September 30 to October 1

Colon and Rectal Surgery

Mayo Memorial Auditorium, University of Minnesota, Minneapolis
(CME) (612) 626-5525

October 5-8

Adolescent Medicine

Earle Brown Center, St. Paul
(CME) (612) 626-5525

October 7-8

Mark Your Calendars!

You are invited to
The Minnesota
Medical Foundation's
50th Annual Dinner Meeting
on the evening of

Wednesday, November 2, 1988

at the

Radisson University Hotel
615 Washington Avenue Southeast
Minneapolis, Minnesota

Featured Speaker:

Elmer L. Andersen

Former Minnesota Governor
and University Regent

6:00 p.m. Reception

7:00 p.m. Dinner and Program

Awards Presentation

Election of Trustees

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