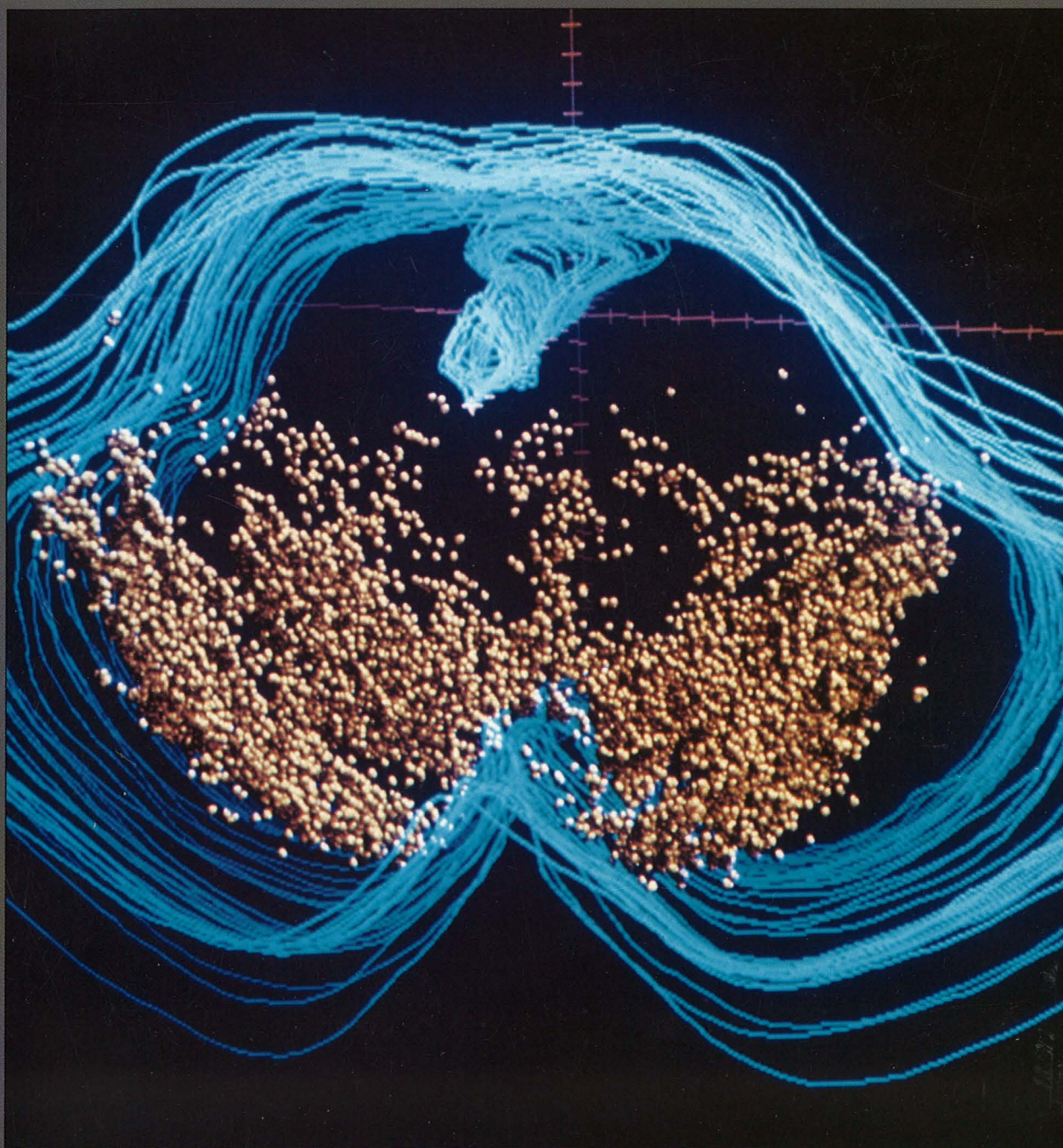


# BIOLOGUE

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER  
AT DALLAS



1987-88



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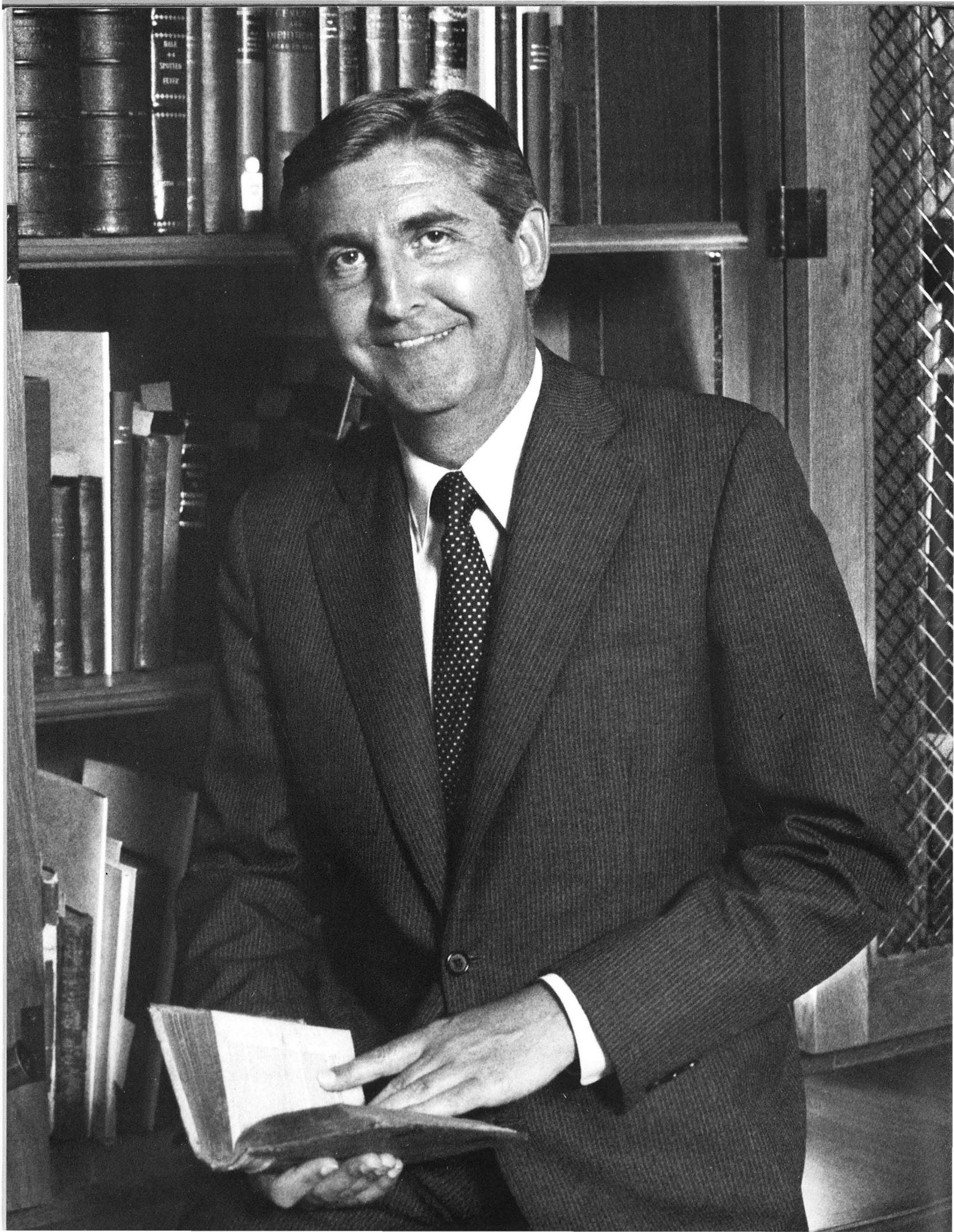
*University Medical Center could have stumbled at the hurdles without the help of high-stepping civic support.*

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**ON THE COVER** Dopamine cells appear to float in three-dimensional space in a computer-generated image formed by taking thin slices of tissue from a normal human mid-brain, designating the location of individual dopamine cells on each slice and then displaying the cell distribution as one image. This computerized cell mapping is the work of Drs. Dwight German, Donald Woodward, Daniel Schlusselberg and Wade Smith.

As part of the health science center's research on schizophrenia, German is testing a theory that schizophrenics have an excess of dopamine. See page 8.







# A MESSAGE FROM THE PRESIDENT

Just a few years ago The University of Texas Health Science Center at Dallas was a small footnote in the list of Dallas institutions—a fledgling medical school begun by concerned community leaders who recognized the importance to Dallas of having a medical school located here. But although our beginnings were modest, the dream of our founders was bold—that this would someday become a medical school of the first order.

That dream took shape over the years and today we have a campus of modern impressive buildings, an outstanding faculty and a student body that graduates consistently in the top 5 percent of their peers in the country. In just over 40 years, we have climbed from obscurity to renown. Two of our faculty have been awarded the Nobel Prize, and we are ranked among the top 10 medical schools in the country by most observers. These are remarkable achievements for an institution as young as ours. Yet, our progress has been incomplete because we have lacked the depth and breadth in referral medicine that all other academic medical centers of the first caliber enjoy.

To achieve full maturity and reach our potential as an institution, we have needed for many years a truly fine private referral teaching hospital on our campus to supplement the excellent clinical care and teaching environment provided by Parkland Memorial Hospital and our other affiliated hospitals. And, once again, community leaders have joined with us in recognizing the need and coming forward to help us achieve our goal. On June 23, 1987, we broke ground for University Medical Center. This 159-bed referral teaching hospital will provide our faculty with a state-of-the-art hospital facility on the campus and enable us to accept referrals from all over the country and the world. We will at last be able to care for a large number of patients who have unusual conditions requiring the special expertise of our faculty, and whose presence will enhance our academic programs in the clinical subspecialties.

University Medical Center will strengthen the potential of our faculty and will enhance our reputation as an institution. It will, in the truest sense, complete the necessary basic components of a great academic medical center. Equally important, University Medical Center will serve to strengthen the medical referral potential and reputation of the Dallas/Ft. Worth area. In addition, it will add measurably to the economic development of our area by bringing national attention to the medical expertise available here, both within the medical school and in all the outstanding hospitals in our region.

We are proud of our heritage and confident of our future. As you read this issue of *BioLogue*, you will learn about some of the programs where research and patient care intersect at the frontier of knowledge, and about other programs that offer expertise not readily available elsewhere in the Southwest. In all instances, our students benefit from an atmosphere in which basic science and clinical medicine complement one another to an extraordinary degree. I hope you will share in the excitement and anticipation we feel about The University of Texas Health Science Center at Dallas and its future.

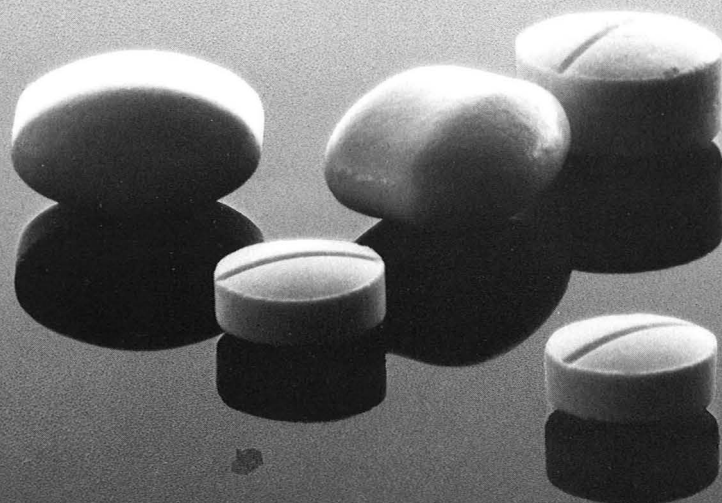
• “University Medical Center  
• will strengthen the  
• potential of our faculty  
• and will enhance  
• our reputation as an  
• institution. It will, in the  
• truest sense, complete the  
• necessary basic  
• components of a great  
• academic medical center.”  
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Kern Wildenthal, M.D., Ph.D.



CALCIUM



# STONES

**"S**ome days are diamonds, some days are stones and bones," read the T-shirts of the UTHSCD mineral metabolism team.



Stones and bones to these researchers means kidney stones and osteoporosis—two calcium-related disorders that lie on opposite sides of the body's delicate mineral balance.

Today, with new treatments developed by this expert group, many patients with kidney stones and osteoporosis can live without experiencing the debilitating effects of their disorders.



**A** smartly dressed professional woman in her late 30s stands outside the clinic door, waiting to have her blood drawn by the nurse. Soon she will take the clinic chair occupied by another patient—a stooped 82-year-old woman, barely four feet tall, who came in clutching a walker with both hands.

Both women are osteoporosis patients, victims of an extreme loss of bone mass due to an estrogen deficiency. And both are at The University of Texas Health Science Center at Dallas to see mineral metabolism chief Dr. Charles Y. C. Pak and his associate Dr. Khashayar Sakhaee.

Thanks to Pak and other members of the mineral metabolism team, both women are now improving. They are

Pak's group has shown that serum fluoride levels can be kept within safe but effective levels. Side effects have been much less frequent and severe than with conventional sodium fluoride preparations.

"Preliminary studies indicate that slow-release sodium fluoride with calcium supplements or active vitamin D can safely make more bone and prevent further bone fractures without causing harmful side effects in persons with established disease," says Pak.

Sodium fluoride is only one of several drugs developed by Pak. Another osteoporosis treatment, a calcium supplement called calcium citrate, has been on pharmacy shelves since 1985. As a dietary supplement, calcium citrate

found in citrus fruit that inhibits kidney stone formation.

Pak and his research group have found that calcium citrate reduces the risk for precipitation of calcium salts in urine that could lead to stone formation. They also have found that calcium citrate is better absorbed through the walls of the intestine than calcium carbonate, the most commonly used calcium supplement. This added bioavailability means that more calcium can be used by the body to make new bone or prevent bone loss.

Having shown the safety of slow-release sodium fluoride and the superiority of calcium citrate, Pak is now testing a combination of the two for its effect on osteoporosis.

B Y S U S A N R U T H E R F O R D

# & BONES

actually making new bone—their brittle bone disease having been stabilized and, in fact, reversed by a treatment program formulated by the group.

The key to the osteoporosis treatment program is an investigational drug, a unique slow-release form of sodium fluoride. Under investigation for the past four years, slow-release sodium fluoride is proving successful in clinical trials at the health science center and at several Dallas hospitals participating as test sites.

Sodium fluoride, a compound used for years by dentists to strengthen teeth, is known for its ability to build bone. "Although there is ample evidence that sodium fluoride can make more bone and prevent or treat osteoporosis, a high prevalence of side effects has precluded its wide usage," says Pak, who is director of the General Clinical Research Center, a mini-hospital at the health science center supported by the National Institutes of Health.

The slow-release form of sodium fluoride was developed by Pak to overcome gastrointestinal and rheumatic complications. Using this compound,

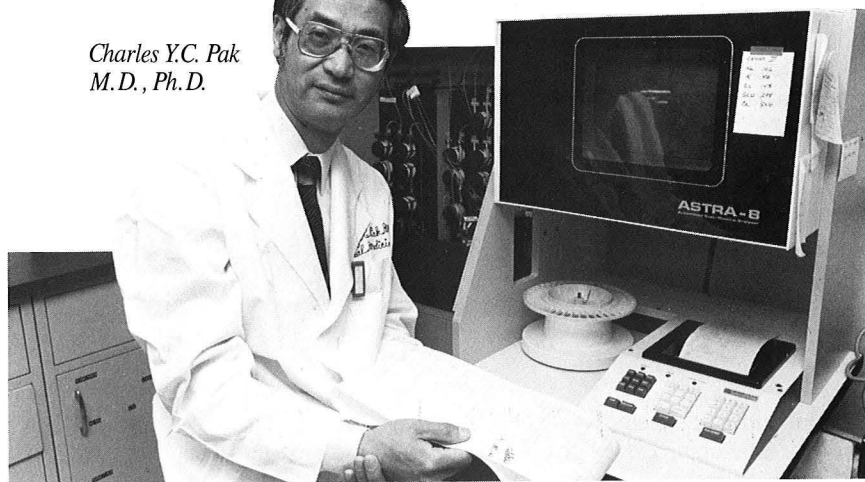
is not considered a drug by FDA standards so it did not have to go through the investigational trial process.

Calcium citrate was designed to strike a balance between calcium's beneficial effect on bone and the potential danger of kidney stone formation caused by too much calcium. Calcium citrate combines the calcium needed for bone formation with citrate, a compound

**M**any people with kidney stones live in constant dread of passing their next stone. The pain is excruciating. Some say it's worse than childbirth.

Most stones form in the kidneys from crystalline calcium salts. Rough and spiny, they cause severe pain as they move through the urinary tract. They may be expelled or they may obstruct

*Charles Y.C. Pak  
M.D., Ph.D.*





# ULTRASONIC BONE SCANNING DEVICE

**T**omorrow's osteoporosis patient may be helped by an invention that looks today like a winning entry in a science fair. The equipment is a "proof of principle" model for an ultrasonic bone scanning device.

The brainchild of physicist Dr. Peter Antich, associate professor of radiology, the new imaging and quantitative equipment holds great promise as a tool for measuring bone strength and elasticity. Together with Drs. Ed Dowdey and Robert Murry, Antich is designing the equipment to help measure the general state of bone in osteoporosis. It also will assess the therapeutic value of slow-release sodium fluoride, the investigational osteoporosis drug being developed by Dr. Charles Y.C. Pak to build new bone in osteoporosis patients.

"We want to know how elastic the new bone is and how strongly it is bound in several dimensions," says Antich. "The most important thing in osteoporosis treatment is not to increase mineral density, but to



*Peter Antich, Ph.D.*

provide sufficient bone strength."

In order to test the integrity of the new bone, Antich proposed using ultrasound because the technique is capable of locating structures within

the body precisely. His ultrasonic bone scanning device will allow the multi-dimensional network of bone crystallization to be measured in both laboratory animals and humans. ■

urine flow and require emergency surgery. Persons having a history of kidney stones can, while undergoing the traditional treatments, expect as high as a 70 percent chance of recurrence.

Helping to reduce this 70 percent recurrence rate has been the goal of Pak's ongoing study, which he started at the NIH in 1968. He has continued the study at the health science center since 1972, supported by the NIH and aided by the Food and Drug Administration.

Rather than treating all kidney stones alike with the traditional "shot-gun" approach, Pak has successfully identified 16 separate stone-forming disorders and has developed selective treatment for each. Pak and his team have developed four drugs for kidney stone prevention. Add to that a medical test kit to aid in assessing a patient's risk for developing kidney stones. And there are several exciting prospects

for the future.

Among the team's many accomplishments in treating kidney stones:

■ Sodium cellulose phosphate was approved by the FDA in 1983 for use in kidney stone patients with "absorptive hypercalciuria." This common kidney-stone forming disorder is frequently associated with increased absorption of calcium from food. While diet modification can often prevent stone formation in the disorder's milder forms, the drug is useful in treating severe forms of the disorder.

During the three years prior to the study, a group of 16 kidney stone patients had passed 372 stones, averaging 7.75 stones per patient per year. During the study, lasting up to five years for some patients, only 11 stones were passed. Eighty-one percent of the patients were in remission and did not form new stones while taking the drug.

■ Potassium citrate, approved by the FDA in 1984, was found effective by Pak's group in reducing the rate of stone formation or stopping stone production in patients with hypocitraturia. This condition is characterized by having a low urinary citrate level, and patients in this group form stones composed of calcium oxalate or calcium phosphate.

In a test group of more than 100 patients with hypocitraturia, 82 percent stopped forming stones while on drug therapy and 98 percent had a reduced rate of stone formation. When treatment ended, the rate of stone formation jumped to its former elevated level.

Potassium citrate, moreover, virtually eliminated the need for surgery due to new stones in these patients. During the three years prior to initiation of treatment, 78 patients had undergone 56 surgeries. Following treatment with potassium citrate for periods of 18

months to two years, only nine surgeries were required, all for pre-existing stones and none for new stones.

Citrate, a substance normally found in urine, is an inhibitor of stone formation since it is capable of preventing the crystallization of stone-forming calcium salts, says Pak. Patients with hypocitraturia are therefore more prone to form calcium stones. In such persons, potassium citrate increases urinary citrate and significantly reduces stone formation.

Hypocitraturia affects about 50 percent of all people requiring medical treatment for kidney stone disease.

Another group who can benefit from potassium citrate treatment are those with gouty diathesis. By increasing urinary pH and citrate, this treatment can avert formation of both uric acid and calcium stones.

The development of this drug was noteworthy since Pak's group conceived the idea, found how the drug worked and tested it for safety and effectiveness—tasks normally undertaken by large pharmaceutical companies.

■ Thiola, a Japanese-made kidney stone drug, was found effective by Pak's group in controlling the formation of cystine kidney stones. The drug, while approved for use in Japan, is undergoing clinical trials in this country for approval by the U.S. Food and Drug Administration.

Symptoms of cystine stones are typically severe. Multiple large stones, often "staghorn" in shape, form in the kidney. And the underlying stone-forming disorder, if unchecked, may sometimes progress to kidney failure and the need for lifelong dialysis. Pak explains that cystine stones are caused by an inherited metabolic disorder, affecting about 10,000 Americans. The disorder is thought to involve a defective reabsorption of cystine into the kidneys. Cystine is an amino acid produced by the digestion of proteins.

Pak and his research team found that the serious side effects that are common among patients taking the standard drug for cystine stones, d-penicillamine, are significantly less common during Thiola therapy. Also, the reduction in urinary cystine produced by Thiola is equal to or better than that obtained with d-penicillamine.

■ The "StoneRisk Patient Profile" is a medical test kit designed to help the nation's estimated half-million chronic kidney stone sufferers assess their risks of forming new stones.

The multi-test kit is intended to assist physicians in diagnosing the cause of kidney stone formation. In so doing, it could help determine the most appropriate form of medical treatment for individual patients. The kit also can be used to monitor a patient's response to drug treatment, says Pak.

Urine samples are sent by the patient to a laboratory, where they are analyzed. A computerized graph indicating levels of chemicals and environmental factors is sent to the patient's physician to aid in diagnosis.

The American Urological Association conferred its Distinguished Contributions Award on Pak this year for his work on kidney stones.

**P**ak's clinical research has won respect nationwide, and he has projects in mind for years ahead. Besides many clinical projects, he plans or has begun basic studies to find out exactly how fluoride makes more bone and why so many kidney stone sufferers have an apparent inherited problem of absorbing too much calcium from their intestines.

However, Pak is concerned about a current trend that sees fewer young investigators choosing futures in clinical research. A clinical investigator applies knowledge gained from laboratory testing to the development of new forms of diagnosis and treatment of patients, as well as to a better understanding of disease processes.

Pak says he works by a system of hypothesis testing. With expertise in physical chemistry and physiology, he and his group have developed a unique way of caring for patients based on rigid scientific methods.

His studies are academically driven, with research as the principal motivator, Pak says. Very little research, if any, has been done solely to promote a drug. Overall research by Pak's group has prospered, as shown by an increasing number of publications (more than 300) and acquisition of research grants.

As a secondary spinoff of that research, drugs have been developed

that benefit patients. And these drugs are proving to be commercially profitable for the health science center.

Collaborating with Pak in many of his drug studies has been the manufacturer Mission Pharmacal Company of San Antonio. Pak and Neill Walsdorf, president of Mission, formed a collaboration in the early 1970s when Pak was trying to find a company to begin making sodium cellulose phosphate, an "orphan drug" that he had developed.

While the NIH has provided much of the support for Pak's ideas and research, Mission has been invaluable in supplying uniquely formulated drugs in a timely manner, Pak says. But Pak and his team currently are working on innovative drug developments with three other companies as well.

In spite of Pak's success in developing drugs and helping patients, he considers the clinical investigator an endangered species. This observation is shared by others at the NIH who have witnessed a sharp decline in the once thriving science of clinical observation. The decline, they say, is partly due to the increasing difficulty that clinical researchers have in obtaining research funds.

"We need a shift in the priorities for which research dollars are being allocated so that more money would be available for clinical research," says Pak. "In a research world now captivated by molecular biology, and rightly so, there is still a place for patient-oriented investigation."

"There are many rewards from clinical hypothesis testing and clinical research. Yet there has been attrition of investigators engaged in patient-oriented research."

Pak wants to help resolve the plight of investigators involved in patient-oriented research, especially young ones. He would like to establish a program to train and support young clinical investigators through private donations and the resources from drug developments.

Pak stresses the need for community involvement in supporting clinical studies. "Important advances from basic research may not be applied toward improved care of patients if we continue to lose people who can do clinical research," he says. ■





JOAN HASSALL  
THE SATURDAY BOOK, 1955

# CLIKE ANCER OF THE MIND

BY ANN HARRELL

WHEN THE VOICES OF THE BIRDS BECOME SO COMPELLING THAT HE CAN NEITHER SLEEP NOR THINK, HE FOLDS UP THE TWO SLEEPING BAGS THAT PROTECT HIM FROM THE FROZEN MOUNTAIN GROUND AND HEADS FOR A PHONE. FROM A BOOTH AT A NEARBY COLORADO TRUCK STOP, HE PLACES THE CALL TO HIS FAR-OFF FAMILY WITH THE LONG-DISTANCE CARD THEY HAVE GIVEN HIM FOR JUST SUCH EMERGENCIES. BECAUSE THEY ARE HIS ROCK... HIS SUPPORT... HIS SOURCE OF LOVE AND HIS ONLY ROPE TO REALITY.

John is schizophrenic. He suffers from a disease that one former patient—now in control—calls “the cancer of the mind.” Like cancer, the word *schizophrenia* strikes fear and dread with its mere pronouncement: the word itself connotes a feeling of doom, an embarrassment, a dark hidden secret. Like cancer, it is also

suspected by modern scientists of being not one, but a cluster of diseases with one emotion-evoking label.

Dian Cox Leighton is a staff member at the Mental Health Association in Austin, Texas, who organizes statewide advocacy programs for mental health and mutual support groups for clients and families. She

herself is a former mental patient who carried the label schizophrenic. Leighton has been treated by numerous psychiatrists and other psychotherapists—not all of whom agreed on the diagnosis of schizophrenia—and has been committed at various times to both private and public hospitals.

Her mother saw her through all of this. “I couldn’t have made it without her or without the support of one of my psychotherapists who made me realize that, no matter how ill I was, I still had to take responsibility for at least some of my actions,” she said. “I think that’s important for patients to know.”

Leighton said that she vividly remembers her mother’s pain at overhearing the word *schizophrenic* unexpectedly. “We were sitting in my doctor’s office while he was discussing the case with a psychologist on the phone. He leaned back in his chair, shot a look at us on the couch and said, ‘Yes, she’s schizophrenic as all get-out.’ Immediately my mother’s hands flew up to cover her face. She wouldn’t look at me.”

Dr. Kenneth Altshuler, chairman of the Department of Psychiatry at the Dallas health science center, believes that “schizophrenia is possibly the most devastating of mental illnesses.” It affects between 1 and 2 percent of the population worldwide, usually strikes down young people in their teens and twenties, claims one out of every five hospital beds in the United States and is estimated to cost Americans \$53 billion a year.

It is reported that only one third of schizophrenic patients get better, one third get only a little bit better and one third do not respond to treatment. Sadly, the last major advances in treatment of schizophrenia were made well over 30 years ago with the development of major tranquilizers.



What is this devastating disease that turns the lives of so many patients and their families into nightmares?

Literature from the time of the ancient Greeks has given us stories of human behavior that we now recognize as schizophrenic. Shakespeare chronicled Ophelia’s quiet retreat

from the dark world of Denmark into her own schizophrenic reality where the gentle language of flowers was spoken. He also dramatized the mad ravings of Lear.

Schizophrenia is a “brain disease” that may have a genetic component, said Dr. Roderick Gregory, UTHSCD psychiatrist and medical director of the Special Diagnostic and Treatment Unit at Dallas Veterans Administration Medical Center, where veterans with schizophrenia can receive treatment.

Disorders of thought and language are common in schizophrenic patients, as is disorganization, said Gregory. “They tend to be hyperactive, can’t follow through patterns in conversation and sometimes invent new words.” Their words may be



*Dian Cox Leighton*

disconnected. There may also be disorganization, lack of motivation, apathy, trouble finishing tasks, “a poverty of words and thoughts” and general unresponsiveness.

Other symptoms are bizarre behavior, strange posturings in public, hoarding food or picking at things. A schizophrenic may think people are talking about him or that there is a plot against him. A schizophrenic may smile when it is not appropriate—like a patient who smiled upon hearing of his mother’s death. Some patients may develop grandiose ideas, such as thinking that they are God or that they tell the president what to do.

No one patient exhibits all these

symptoms, said Dr. Joachim Raese, UTHSCD psychiatrist and director of the Schizophrenia Research Center at the Dallas VA medical center. However, mental health professionals usually either categorize schizophrenia as “paranoid” or “non-paranoid” or categorize it by behavioral symptoms, with “plus” indicating acting-out and “minus,” retreating behavior. They admit these are only pragmatic guidelines that do not deal with the complex realities of schizophrenia.

Nor do all patients remain in their convenient diagnostic categories. It is not uncommon for the quiet schizophrenic after years of illness to undergo a sudden metamorphosis into the “crazy” or “acting-out” type of patient. This does not mean that the patient is violent, however; the behavior change may be such that the patient does things that call attention to himself in a peculiar manner. In fact, there are few violent schizophrenics.

With the emergence of Freud’s theories and their influence on the treatment of mental illnesses in this country, there was a shift from viewing these conditions as physical aberrations to examining the psyche. Psychotherapists sought causes in damaging childhood experiences and sought “cures” in the resolution of conflicts, which often occurred in childhood. Because of these emphases, parents of schizophrenic patients often paid a heavy price in guilt.

Now much of the thinking about mental illness has changed. “In more recent times the biological model has been shaped by the growth of the . . . neurosciences,” wrote psychiatrist Nancy C. Andreasen in her book *The Broken Brain*. Andreasen defines neuroscience as a “combination of a set of related disciplines that have the common goal of understanding the relationship between brain structure and function, and human thoughts, feelings and behavior.”



Psychiatrists at the health science center launched a multimillion-dollar biobehavioral brain science program to investigate the biological components of mental illness two years ago.



The project draws from research in other departments, such as neurology, cell biology, biochemistry and others, said Altshuler.

Some of the work referred to by Altshuler is taking place in the laboratory of Dr. Dwight German. The researcher is using computer imaging techniques to study the number of dopamine-containing nerve cells in the brains of normal and schizophrenic individuals and the three-dimensional distribution of the cells. This work is designed to test the theory that schizophrenic patients possess too many of a specific population of dopamine-containing nerve cells.

It had earlier been noted that patients suffering from Parkinson's disease had a deficiency in the number of dopamine-containing nerve cells in a motor-related portion of the brain. This disease is characterized by slowness of movement, muscular rigidity and resting tremor. Doses of L-dopa, a dopamine precursor that is converted into dopamine in the brain, successfully compensate for this chemical deficiency when administered to patients with Parkinson's disease. However, it was found that excessive doses of L-dopa often gave rise to schizophrenic symptoms, such as hearing voices that instruct patients to perform actions they feel they must carry out—sometimes even to the point of suicide.

This discovery has given rise to the theory that schizophrenia is caused by an excess of dopamine in certain brain regions. Today the major drugs of treatment are dopamine antagonists, or "blockers." Unfortunately, these drugs decrease the amount of dopamine in the entire brain and often cause patients to develop some of the symptoms of Parkinson's disease—in many cases a bitter trade.

"All of these neuroleptic drugs have significant side effects," said Raese. The patient may experience painful involuntary muscle contraction, sudden stiffening of the muscles, his eyes' rolling up, an inability to stand still, tremors or other sometimes intolerable symptoms.

Meanwhile, researchers continue their search for more effective medications with fewer side effects.

Catherine Judd, coordinator of clinical research in the unit, is involved in running clinical trials with new anti-psychotic drugs.

Developments in modern technology have brought about new ways to look into the human brain that may help unlock the doors to the causes and cures of schizophrenia. One development is "dynamic imaging," so called because it enables researchers to study the brain in action. Raese and his associates are teaming up with researchers in the Nuclear Medicine Center to use dynamic imaging to learn more about what happens in the brains of schizophrenic patients.

Dynamic imaging uses a single photon emission computer-assisted tomographic scanner, which was developed in Denmark through a collaboration of UTHSCD and Danish scientists. Xenon-133 gas is used to track the brain's blood flow

## **T** HIS BIOBEHAVIORAL BRAIN SCIENCE PROGRAM INVESTIGATES THE BIOLOGICAL COMPONENTS OF MENTAL ILLNESS.



and has distinct advantages, say UTHSCD researchers. These researchers have become well known for their studies of the brain using the xenon technique. In fact, Dr. Ernest Stokely, UTHSCD nuclear medicine researcher, was a co-developer of this machine with Dr. Niels A. Lassen. The machine at the Dallas health science center was the first in this country and only the second in the world developed for this technique.

Raese and his associates, Gregory and Dr. Ronald Paulman, team neuro-psychiatrist, became interested in the potential of this technology and went

on to investigate abnormalities in the brains of schizophrenic patients. They joined forces with research radiologists to see if the abnormalities could be confirmed by xenon studies that depict blood-flow images in color. Dr. Frederick Bonte, the director of the Nuclear Medicine Center, and Dr. Michael Devous, who directs the schizophrenia imaging project, began doing blood-flow studies with schizophrenic patients from the VA medical center in collaboration with Raese and his associates.

This collaborative work in the Nuclear Medicine Center at UTHSCD focuses on abnormal blood-flow patterns. One of the first studies involved 40 patients, half diagnosed as paranoid schizophrenic and half non-paranoid schizophrenic; half of the 40 took dopamine suppressants and half were free of medication. Young patients were chosen so that the effects of long-term medication would not compromise the picture of brain activity. The blood flow in their brains was "photographed" while they were at rest.

The color-coded slides of three brain slices indicated that there were indeed statistically significant abnormalities. Not only was the blood flow to the frontal lobes low, but the paranoid patients were three times as likely to have low frontal blood flow. The results seemed to be independent of medication.

In addition, the study showed that there were other biological differences. There was also a tendency to low blood flow in the temporal lobes in both the paranoid and non-paranoid patients, and blood-flow patterns in the entire brain were higher than in normal controls who had been studied in the Nuclear Medicine Center. This finding gave rise to the speculation that perhaps the schizophrenic brain is overactive, said Raese.

The research team is also investigating whether information is processed differently in the frontal lobes of patients who have schizophrenia. Paulman is collaborating with Dr. John Herman, UTHSCD psychologist, using the Wisconsin card sort test, in which subjects have to sort cards into several different patterns.

Although the patient is lying down inhaling xenon through a mouthpiece, he is able to perform the test by using hand signals to the researchers as he sorts in his mind.

Researchers found that the blood flow literally shut down in the frontal lobes of the paranoid patients when performing the card sort. "Major flow reductions showed up where there had been blood flow," Devous reported. At the same time, blood flow in the rest of the brain seemed activated. Conversely, blood flow showed normal or increased activity in the frontal lobes of all but one of the patients diagnosed as non-paranoid schizophrenic.

The test gave strong indications that there are differences in the way the brain works in paranoid and non-paranoid schizophrenic patients. In performing the card sort, the paranoids did poorly. The non-paranoid schizophrenics didn't perform any better on the test; however, their brains' frontal lobes activated while they were trying, as shown by the increased blood flow.

No consistency was found in the patterns of normal controls tested on the Wisconsin card sort. Some had blood-flow patterns that went up while some went down. Devous said that more study is needed to understand why this happened.

The researchers are excited about a new tomographic scanner called the TRIAD that will have much better instrumentation than the currently used machine. After the TRIAD is received in mid-1987, the group will begin studies that will "tag" dopamine receptors, opening up the possibility for learning more about the production of dopamine and its relationship to schizophrenia. Studies are also planned to look at other receptors that have been identified and at their "tracks" to see if there are any implications for schizophrenia.

Another way of looking at the brain is electrically, said Raese. Called topographical EEG mapping or brain electrical activity mapping, this procedure uses electroencephalogram bands to gain information. It processes the data and displays the information as a varying band of electrical impulses, usually traced on

# A

## ALL OF THESE STUDIES GIVE RISE TO THE HOPE FOR BETTER TREATMENT OF SCHIZOPHRENIA IN THE FUTURE.



paper. Raese, in cooperation with Dr. Kenneth Pool, a neurologist, uses this new tool in conjunction with the brain blood-flow images.

Other UTHSCD studies on schizophrenia include work by Dr. Joel Steinberg. Steinberg is studying HVA, a dopamine metabolite in the blood of schizophrenic patients, hoping to find a predictor for improvement. Another collaborative effort of the Schizophrenia Research Center involves Dr. Donald Capra, professor of microbiology and internal medicine. Capra has found unusual patterns in the DNA of diabetic and multiple-sclerosis patients and is trying to determine if this is also true of schizophrenics.



All of these studies give rise to the hope for better treatment of schizophrenia in the future. But what about today's victims in our hospitals, on our streets or hiding out in their family homes?

Dr. Douglas Puryear, health science center psychiatrist who is in charge of the Parkland psychiatric emergency room, said that possibly things are better today than ever before for patients with schizophrenia and their families.

Puryear sees his job—and the job of the other mental health workers in the emergency room—as evaluation and crisis intervention. They first give a medical examination to determine if the problem may be caused by another underlying illness, such as diabetes or

a brain tumor, before giving the accepted diagnostic psychiatric exam, the DSM-III.

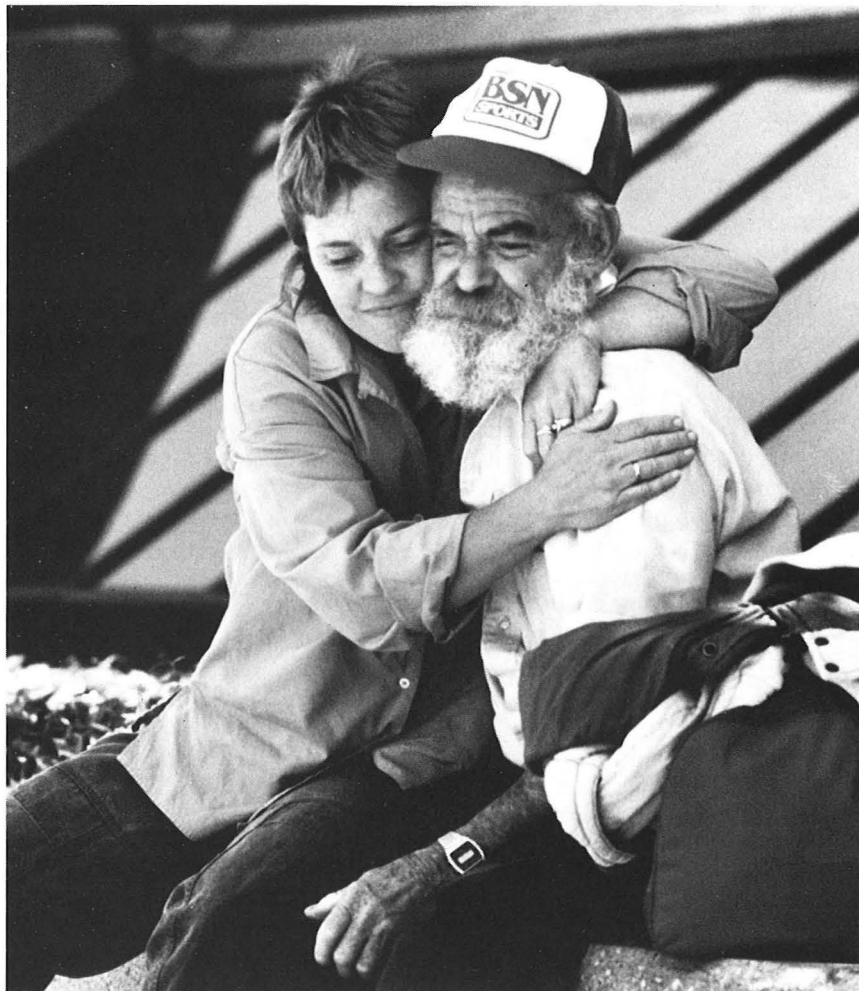
"With schizophrenia," says Puryear, "patients usually need to be stabilized on medications, and the family needs help." The psychiatrist is a believer in self-help groups for both patients and families. He often makes referrals to Family and Individual Reliance (FAIR), the group Dian Leighton works with, and to the Dallas branch of the Alliance for the Mentally Ill (AMI), led locally by civic leader Maura McNeil. In addition, he sees private patients with schizophrenia for psychotherapy and works with family groups. Currently he is involved in research on the ability of family groups to relieve stress.

Puryear said he believes Dallas is doing a good job for patients in spite of limited resources. The last state legislature mandated reforms for mental health but adjourned before voting funds. There are long waits in the emergency room and often no follow-up. However, the psychiatrist pointed out that there are many organizations throughout the city who form a network to find the best help possible for a schizophrenic patient.

Not only are state, county and city resources stretched, but schizophrenia is a financial nightmare for all but the richest members of society. If a patient has unlimited funds or insurance, then private hospitalization is a possibility, but even the most liberal insurance policy reaches its psychiatric limit quickly. Then if there is no money, state hospitalization or discontinuation of treatment may be the only option.

Although the stereotype from *The Snakepit* still lingers in the minds of many, both Puryear and Altschuler report that patients at Terrell State Hospital, the nearest state mental hospital, are receiving much better care than in the past. In fact, this year a health science center psychiatry faculty member, Dr. Barry Fenton, was appointed medical director for Terrell in an effort to work more closely together. Today that hospital probably has the best staff-to-patient ratio in its history. However, it does not have to treat patients who are not extremely ill so the problem of a





*Carl, one of the homeless who suffers no mental illness, still appreciates the friendly attention of Kay Peterson, psychiatric nurse to Dallas' street people.*

patient's being kept in a state hospital beyond need is pretty much a thing of the past.

Today's problem arises from releasing patients who have no place to go. Cecile Bonte, director of the Mental Health Association of Dallas County, is one professional who is acutely aware of the problems of patients and their families. The Mental Health Association is a coordinating agency that acts both as a clearing-house for information and referrals and as a major source for public and professional education. It is involved daily with schizophrenics and their families. Housing is a major concern since many patients have no families or their families have given up on them. Very few shelters and boarding houses exist in the community, yet 30 to 40 percent of the "street people" are thought to be victims of schizophrenia.

In addition, the Texas Mental Health Association, under the leadership of Stella Mullins, formed a task force to study the needs of mental patients in Texas at the request of the state legislature, a first for a private agency.

Another source of help is the Mental Health and Mental Retardation Center of Dallas County. A major goal of MH/MR is to keep patients out of the hospital. Social workers there aim to help recently released patients (60 percent of whom are schizophrenic) become self-sufficient in 90 to 100 days. They help the patients with medication maintenance, job training and placement, housing and other problems, such as applying for disability payments if their schizophrenia makes it impossible to work.

Unfortunately, MH/MR has undergone drastic funding cuts over

the years. In its early days it was eligible for matching funds from the state and federal governments. With federal funds drying up for social programs, the agency finds itself in a difficult situation. The county claims services should be financed by the city and the city points its finger at the county, reported the MH/MR director, Dr. James E. Kraft. In addition, existing funds have been strictly limited for services to the severely mentally ill.

The Stewpot, run by the First Presbyterian Church, is a major refuge and temporary shelter for street people, where a free lunch is always available. Besides the staff and volunteers who are at the Stewpot daily, two dedicated mental health professionals spend a great deal of time there. They are Terry Paul, a former wartime jet mechanic who returned from Southeast Asia with a desire to do something for people, and Kay Peterson, a City of Dallas psychiatric nurse.

The burly, bearded man and the tiny nurse work beautifully as a team administering aid to the city's street people and other disfranchised citizens through the Dallas Community Outreach Coalition, which is sponsored primarily through private funds. This psychiatric health team sees about 140 men and women in a three-month period. One of their toughest jobs is to gain the trust of the people they are there to help.

Encouraging the patients to stay on their medication and ensuring they make follow-up doctor's appointments are important parts of their job. Besides being available at the Stewpot most days, the two have regular medical clinic hours at the Austin Street Shelter, Dallas Life and the Union Gospel Mission. Helping take care of these people's physical as well as psychological ills is an important part of their day.

Yes, resources are severely limited. And sometimes the system is hard to crack. But things are going to get better for mental patients because there are a great number of dedicated professionals out there working to see that they do—and they're all working together. ■

Imagine overcoming a tremendous hardship in one period of your life, simply to have it return at another time. Imagine being 45 years old and, after 40 years of near-normal life, suddenly being unable to walk. Imagine succumbing to what you managed to conquer as a child—polio.

For some people, this is reality. Many of the estimated 300,000 polio survivors are experiencing a sequel to the original viral disease—post-polio sequelae. The symptoms of post-polio include progressive muscle weakness, muscle atrophy, fatigue and joint pain. Some of the more severe cases include respiratory problems and intolerance to cold.

Post-polio can affect any person who survived polio, but those most likely to have symptoms are the ones who were hit hardest by the virus originally. It is estimated that between 50,000 and 60,000 polio survivors are experiencing post-polio sequelae.

Dr. Roger Rosenberg, chairman of the Department of Neurology at The University of Texas Health Science Center at Dallas, says that in order to understand the possible explanations of post-polio one must first look at the polio epidemics of the 1940s and 1950s.

Poliomyelitis is a progressive viral disease. In the early stages of infection, the poliovirus attacks the anterior horn cells, or

# The Sequel

## No One Asked For



*Karen Miller, 1955  
and today*



**By Diane Adell**



motor neurons, of the spinal cord. Rosenberg says, "When a nerve cell in the brain fires a signal to a nerve cell of the spinal cord, in healthy people this signal should continue on to a muscle. However, if a nerve cell in the spinal cord is damaged, the message will never reach the muscle, and muscle weakness or paralysis results." Once a nerve cell dies, it can not be regenerated; therefore, poliomyelitis can leave its victim partially or completely paralyzed.

Polio victims were able to regain varying degrees of muscle strength through physical therapy, depending on the extent of nerve cell damage. For example, if a victim were confined to a wheelchair, it could be assumed he or she would never walk. If the therapy required only a brace, however, the polio victim could work in hope of eventual freedom.

**W**hy are so many of these survivors reliving what they thought was a past chapter of their lives? The currently accepted theory is based on how polio survivors, many of whom were in their early teens, responded to their disabilities physically and emotionally. Did they fight the weakness or accept their motor dysfunction? Did their adolescent self-consciousness dictate their actions? Did they continue to see a physical therapist or decide to make it on their own? Each individual's approach may have affected his or her chance of experiencing post-polio sequelae.

Physically, polio survivors had a serious problem. They lost anywhere from a few to nearly all motor nerve cells. However, in some cases neighboring cells assumed the responsibility of the damaged cells and supplied stimulation for more than their normal share of muscles.

Rosenberg explains how this could happen: "For example, one nerve cell sends messages to muscle fibers numbered one, three, five, seven and nine. Another nerve cell reaches fibers numbered two, four, six, eight and ten. If the first cell is killed by the poliovirus, the second cell may overextend and sprout to fibers five and seven but not to one, three and nine. The second cell takes over most of the territory of the dead cell but not all of it."

This nerve sprouting resulted in a

gradual increase in muscle strength—the polio survivor regained movement. For many survivors this symbolized victory; they had won.

Marge Barré, associate professor and assistant chairman of physical therapy at UTHSCD, says the compensating nerve network functioned properly for a couple of decades, but eventually time took its toll. Over the years, added stress on these nerve cells created "overload." This overuse scarred or destroyed the cells and, many researchers believe, resulted in post-polio sequelae.

Many polio victims have felt the initial effects of overload: fatigue and weakness. Over time the symptoms worsen; lacking replacement nerve cells, the post-polio victim cannot get stronger. As Barré says, "The post-polio victim begins to experience the aging process nearly 20 years before his time."

The reasons why some polio survivors are afflicted with post-polio sequelae while others remain symptom-free are not clear. Many researchers believe that polio survivors who discarded their braces early in life and continually wore down their joints and muscles were probably complicating problems by increasing the stress on muscles and nerve cells. The braces, if worn, may have served as protective cushions lessening the overload.

Dr. Vert Mooney, chairman of orthopedic surgery at UTHSCD, says, "Some of the problems are based on the fact that, lacking braces, these people developed deformities from years of walking without support."

But Mooney and Barré agree that there is uncertainty surrounding this theory. Barré says she has a patient who continually wore a brace and attended physical therapy sessions after being afflicted with polio. "She is in as good shape now as she was at the time she was discharged. But we have no way of knowing if everybody would have reacted in the same manner."

Mooney, looking at the situation from a humanistic point of view, adds, "Why would these people want to wear their braces? They were getting along well without them, and they couldn't stand wearing them. Also, there may have been a useful trade-off because the braces were very heavy and required

additional energy for movement. The cost versus the benefit is negligible."

Psychological factors also may have contributed to the likelihood of experiencing post-polio symptoms and to the extent of muscle weakness and pain. The overachieving attitude taken by or urged upon polio survivors may have influenced their lives to a great extent.

Physicians, family members and friends were simply following the accepted theory of the time when they urged polio survivors to fight their handicaps and prove they were capable of accomplishing what the next person could. Dr. Gene Swenson, rehabilitation psychologist at UTHSCD, says, "Polio survivors were told that they would have to work hard if they wanted to succeed. Many of these people took on aggressive, action-oriented lifestyles and were able to function without braces."

Polio survivors spent nearly half a century fighting handicaps that would have been easy to succumb to. Now, after many have attained the lifestyles that most healthy people take for granted, post-polio victims are instructed to change the habits that brought about their success.

Many researchers believe that post-polio victims are simply aggravating their situation by keeping up the physical pace they have had for years. "Whereas the usual philosophy is 'it will get stronger if you exercise it,' in the post-polio situation this is not true," Mooney says. Too much exercise for these people may be the source of additional disability simply because of the lack of strong functional nerve cells and the absence of replacement cells.

Swenson explains that it is very difficult psychologically to change a lifetime habit, especially one that has been of so much benefit. "This realization of extreme change is frightening, maddening and frustrating. It is a challenge to one's sense of identity. Imagine being 50 years old and feeling 75. Most of us age gradually and come to grips with it. These people are experiencing a time warp, a speeding up of the aging process."

**K**aren Miller is experiencing post-polio sequelae. Miller, a patient of Barré, had polio when she was in the ninth grade. She

remembers, "Everyone kept saying, 'Come on, you can do it. You can get rid of this brace.' And when I did, I believed the treatment was successful."

"A few years ago I began feeling tired. Gradually I was experiencing more pain. Then, one day I couldn't put any weight on my leg. Marge Barré tested my strength, and she couldn't believe that I had enough muscle power

to wear a brace again to combat any further problems. "People experiencing post-polio need to protect what they have. The brace is a small price to pay. The newer braces are lighter and more cosmetically acceptable than the ones most polio survivors remember wearing."

Miller used to try to fight her muscle deterioration, but she now wears

doctors of the '40s. "Many physicians today were not in practice when the epidemics hit and haven't had the opportunity to see and work with polio. Most of the doctors who treated polio are no longer alive, and any doctor who is not knowledgeable about a disease is at a loss to counsel a patient. There is no one to blame; it's a 'Catch-22' situation."

In some post-polio cases there are

other tensions making the experience even more stressful. Many spouses and families don't accept what is happening to their loved one. In other situations the post-polio victim has hidden negative feelings that date back to the original experience. Swenson says that many people never came to grips with the initial polio experience; therefore, they are having difficulty accepting the return of similar symptoms.

Recently several

professionals and organizations have made their services available for post-polio victims. The first step to self-help is to see a physical therapist or a psychologist. These professionals can help an individual assess his or her personal situation.

Another source of encouragement is the Dallas Area Post-Polio Association, founded by Carol Williams. DAPPA, which has grown from 38 to more than 700 members in less than three years, meets bimonthly to exchange ideas and information.

Mooney notes that post-polio victims have difficulty taking the first step toward improving their physical problems because, as Miller experienced, taking responsibility for one's condition is an acceptance of one's disability. He says, "No one enjoys perceiving himself as being disabled. The burden the handicapped person feels of not being normal leads to a real depression, especially since these people have had to stretch their emotional energy further than most normal people. It is an interesting example of the human spirit working." ■



Vert Mooney, M.D., Marjorie Barré and Gene Swenson, Ph.D., (from left) work with post-polio patients.

to walk from my car to her office."

Miller explains that polio survivors like her have developed personality traits that resist a decline in physical activity. Even when she felt very fatigued, she would still exercise, put in a full day of work, make dinner and do household chores. "The 'go get 'em' attitude is still prevalent. Even on my day off, when I should take a nap, I make a list of things to do. If I don't finish, I won't take a nap. And now I'm told to change my lifestyle completely. It's very difficult to slow down, especially after all these years."

In spite of the frustrations, Miller laughs as she discusses the idiosyncrasies of her condition. She is one of the exceptional people who can be honest, yet humorous, about her situation. "Shoes were and still are very important to me because I could never wear fashionable shoes with my brace. I had to wear ugly brown oxfords to my first formal dance! Even years later, when I found out that I needed a brace again, I immediately said, 'No,' because of the association with ugly shoes."

Barré stresses that many post-polio victims need to use canes or crutches or

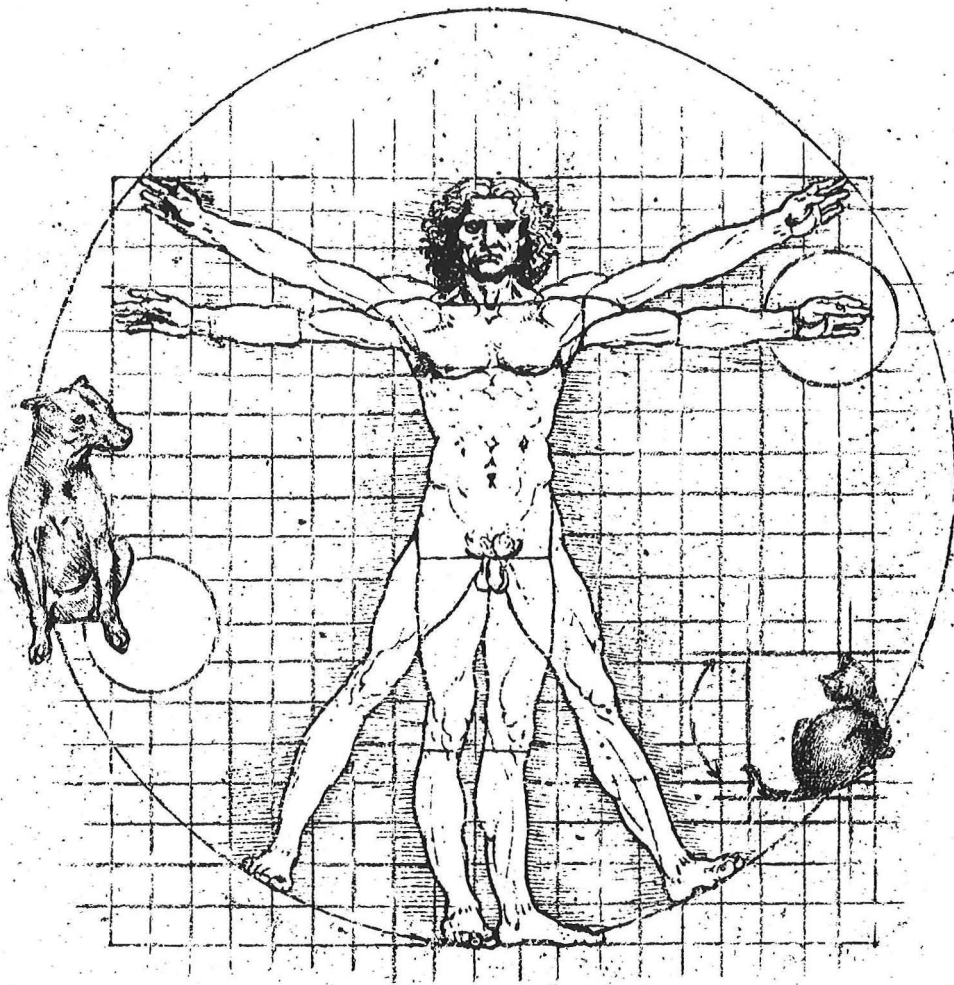
a brace and her favorite shoes. "If you can't change something, you really have to accept it because fighting the inevitable isn't worth it. Talk about feeling fatigued—you are really worn out when you don't accept where you are and what you need," she says. "It is like finally agreeing that you are handicapped."

Barré says that post-polio victims have to be honest with themselves and what they are experiencing. But, unfortunately, many of these people are not getting the facts that will allow them to evaluate their situation objectively. Some even meet frustration where they should find understanding—in the doctor's office.

Miller went through a traumatic period trying to locate a doctor who would even agree to see her. "I called at least 25 offices. I explained that my right knee hurt as a result of polio. The receptionist said, 'The doctor doesn't see people like you.' When you find out that people aren't willing to talk to you, you feel like some kind of freak."

That scene is not uncommon for post-polio victims. Barré explains that the doctors of the '80s are not the





# A Proper MODEL of MANKIND

BY ANN MC VAY

**T**he brown and white beagle bounds in the door, white-tipped tail wagging. She paces the floor excitedly, eyeing the fan at the end of the treadmill. Dr. George Haidet, assistant professor of internal medicine, flips the switch and turns on the fan.

Hardly waiting for her cue, Eight-ball, the beagle, leaps onto the treadmill, ready to run. As a participant in a cardiovascular study being conducted by Haidet, she has worked out on a treadmill for several months.

"Good girl." Haidet pats her flank, quietly encouraging the dog, and her feet pick up a bit. As she nears the end of each exercise session, she is urged to run the last few yards by friendly pats and words of encouragement from Haidet and the rest of his staff. Eight-ball has built up to one hour every day.

Preparing to check the dog's heart rate, Haidet adjusts the transducer that is attached to an aortic catheter extending from her neck. The thermal stylus jumps. "Two hundred forty-five beats per minute," says Haidet. "That's about 85 percent of her maximal heart rate." Like any other trainer, Haidet constantly evaluates the effects of his athlete's workout.

Three-year-old Eight-ball, equivalent in age to a 21-year-old human, is one of several young dogs that will provide a baseline adult comparison for the same tests that are being conducted on geriatric beagles, from ages 10 to 14 in dog years, or 70 to 98 by human standards. The purpose of the study is to understand the effects of age on the function of heart and blood vessels.

"Functional capacity declines in all of us as we get older," Haidet says. "Our ability to do work—to run and to lift weights and perform all kinds of activities—diminishes with age. It's still not very well known what causes that decline in our functional capacity.

"We need to define the effects of aging itself, to separate them from the effects of disease processes. The prevalence of coronary artery and vascular disease increases in people as they age. That makes it difficult to determine which changes in cardiovascular function are due to the effects of disease processes and which changes are due to the effects of aging."

Because dogs have a low incidence of coronary artery disease and atherosclerosis, they make excellent subjects for research on aging. Haidet is able to determine the effects of age without a concurrent disease process.

"Surprisingly, we're seeing that during strenuous exercise the old animals seem to be able to send blood to locomotive skeletal muscles, the exercising muscles, as effectively as the younger animals do. But they do so at the expense of blood supply to different organ systems," Haidet says. The renal or kidney system, especially, appears to receive less blood flow, as well as the spleen, stomach and intestinal areas.

Since humans have a high incidence of atherosclerosis, they would not be as good for Haidet's research purposes as dogs, even if it were feasible to follow humans over a long period of time. In fact, considerations of time, expense and safety cause scientific investigators to use "models" for most of their research.

"In selecting an appropriate research model, the investigator looks for a simplified example of the object or process under study," according to a National Research Council directive in April 1985. "A model is, in effect, a substitute, or analog, for the principal object of interest. . . ."

Researchers may find an appropriate substitute in an *in vitro* cell culture, in a computer statistical model or in an animal. Sometimes there is no substitute for man, and then clinical research involves the observation or treatment of patients. In any case, the ultimate validity of any study depends on choosing the proper model.

Not so far away from Eight-ball, the UTHSCD champion weight-lifter, a mottled cat named Edith, reaches out with her forelimb and moves a 1.2 kilogram weight, more than 50 percent of her body weight. While Haidet attempts to understand why muscle capacity gradually diminishes with age, Dr. William Gonyea, acting chairman of the Department of Cell Biology and Anatomy and dean of the School of Allied Health Sciences, proves that muscle can not only grow stronger but actually increase in mass.

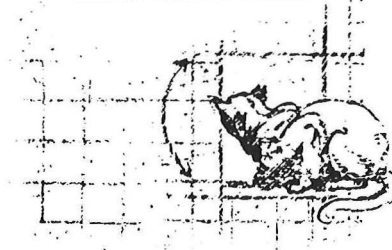
In order to induce muscle hyper-

trophy, or enlargement, Gonyea puts adult cats through an exercise regimen for 30 minutes a day. Using a positive reward system, Gonyea insures that the cat always exercises with the same forelimb.

"They use one limb for exercise. The other one is the control," explains Gonyea. Like a human, a cat favors either its left or right side. Once the cat's

"In selecting an appropriate research model, the investigator looks for a simplified example of the object or process under study. . . . A model is, in effect, a substitute, or analog, for the principal object of interest. . . ."

National Research Council



dominant side is established, the cat gets no reward for using the wrong paw.

"Cats are like humans in the way they use their forelimbs," Gonyea says. "They manipulate forelimbs like we do. Cats also have similar motor skills."

In addition to being appropriate research models, cats are easy to work

with and are fairly easy to train, he says. But like some humans, some cats are not motivated to exercise. Each has an individual personality. Training may take from two days to two weeks.

"Siamese cats don't do well," says Gonyea. "They are very stubborn. It doesn't matter how hungry they get, they won't touch the bar. Long-haired, big, fluffy cats don't do well, either."

But Edith, a calico cat, has confirmed for Gonyea that hypertrophy can and does occur. Her forelimb muscle has expanded by 50 percent in weight since the experiment began.

"What is most controversial about this," Gonyea says, "is that the cat is supposed to be born with all the muscle fibers it will ever have." The same is assumed to be true for humans. Gonyea is convinced that hypertrophy is not due solely to stretching of muscles, as some other research findings have suggested. His data indicate that the muscle fibers have actually increased in number as well as size.

The next step of research has led him to another animal model. "We've started with the Japanese quail, using the wing as the forelimb. We put a weighted collar on a wing. One of the muscles that resists this and tries to lift the wing is the *latissimus dorsi*."

For a month, the plump, pearly Japanese quail, each weighing about 150 grams, resemble human athletes wearing wrist weights. "With the quail, the muscle fibers involved are increasing in mass by 300 percent within 30 days. That's 300 percent versus 20 percent in the cats in one year."

Through continued studies of the cats and quails, Gonyea hopes to explain the controlling mechanism that regulates the process of muscle growth. "Are humans capable of increasing in muscle mass to the extent that we see in the quail?" he asks. "Could we, perhaps, learn to stimulate whatever regulator it is that might induce the formation of new muscle for patients with extensive injuries?"

Of no less importance in animal research are the different strains of rats and mice used by UTHSCD investigators. A bit less endearing than Eight-ball the beagle and Edith the cat,





George Haidet, M.D., clocks Eight-ball on the treadmill in his research on cardiovascular function.

rodents are, nonetheless, the models most frequently used for significant research projects at the health science center.

Some animals are particularly suited for certain studies. Dr. William Pettinger, professor of pharmacology and internal medicine, uses rats for his studies in high blood pressure. The choice was automatic. "Abnormalities in hypertension in humans are so similar to those in genetically hypertensive rats," says Pettinger. "For example, their kidneys retain excess sodium, and high dietary sodium intake contributes to their high blood pressure as it does in humans. Also, the genetic background is a major factor that determines blood pressure level and response to dietary sodium. It is clearly the closest animal model to us in respect to hypertension. The rat is one of the few genetically hypertensive models."

As part of his investigation, Pettinger and his colleagues work with kidneys removed from rats, one at a time. Each kidney is oxygenated by a pediatric dialysis coil, much like an artificial kidney for a child. The kidney, while perfused with a plasma substitute, functions drop by drop.

"By taking that kidney out and perfusing it in a controlled environment,

we are removing it from many circulating hormones and nerve systems that might influence it. In this way, we can study the effect of each hormone singly."

Kidney tubules have receptors on their surfaces that attract and bind certain hormones. The hormones activate a series of responses known as intracellular signalling. First the hormones stimulate an enzyme, adenylate cyclase, to produce a "second messenger," cyclic AMP. This second messenger signals the cell to increase or decrease its sodium and water excretion.

Pettinger has observed that genetically hypertensive rats have defects in the mechanisms for receiving and transmitting signals from the cell's surface to its interior. The defects result in inappropriate responses.

For example, some rats with genetic hypertension have more receptors for adrenaline and a greater affinity for the hormone than normal rats, particularly when the rats are on a diet high in sodium. Pettinger is using the perfused rat kidneys to find out how abnormally regulated receptors for adrenaline are related to genetic rat hypertension and, possibly, to human essential hypertension.

Through other research, Pettinger has explained how, under certain con-

ditions, the hormone vasopressin becomes salt-retaining instead of salt-excreting. Last year Pettinger traced the reversal to a specific site in the kidney tubule.

The findings will not radically change present treatment of hypertension, Pettinger says. "We're not yet preventing high blood pressure. But once the altered regulatory mechanisms are understood, approaches to the solution will rapidly evolve."

That researchers often use rats and mice as "substitutes" is a matter of practicality as well as appropriateness for the project, says Dr. Steven Pakes, director of the Animal Resources Center. Researchers may have several choices of animal models and have to decide which is best for that particular study.

"Investigators will generally use the one that is lowest on the phylogenetic tree — the lower forms of animals. If all other factors are the same, cost will be a consideration in choosing the model," Pakes says. "Mice are cheaper to keep, easier to work with because of their size and are especially good models for those investigations that require genetically pure animals.

"And they're not going to use monkeys when they can get the answer in mice or dogs," Pakes adds. But the decision must be weighed carefully. If the investigator proposes using mice because they are cheaper when the rabbit is known to be the better model for that type of research, he will not be funded.

Investigators often incorporate *in vitro* models in conjunction with animal research. Working with a cell system is preferable to sacrificing an animal; yet tissue cultures, though living, are a controlled and somewhat artificial medium. They cannot always yield the comprehensive answers that may be obtained by animal experiments.

The investigator's medium, his "work place," is never constant, according to Dr. Robert Tigelaar, associate professor of dermatology and internal medicine. "The model that you need changes, depending on the question that's being asked. If the appropriate question can be answered in man, that's

ideal; but after that, it depends on the question. Some questions can't be answered *in vitro*. Some can only be answered *in vitro*." Tigelaar has used mice for studies of atopic dermatitis, or eczema. Individuals who have eczema frequently also have asthma and/or hay fever; they usually have elevated levels of IgE antibodies to many environmental allergens. "But while asthma and hay fever are known to be triggered by such allergens interacting with IgE antibodies," says Tigelaar, "the mechanisms that lead to dermatitis have remained a mystery. Furthermore, no suitable animal models or *in vitro* systems have been developed to solve the mystery."

Tigelaar has applied allergens directly to the ear skin of a mouse that has been given high levels of IgE. The measurements of the swelling produced by the antibody interacting with the allergen, in conjunction with related culture studies, may provide a closer understanding of the mechanisms involved in this common skin disorder.

"*In vitro* models are advantageous because they allow you to dissect more precisely a complex system that is composed of several parts," says Tigelaar, who employs both tissue culture and animals. "You need ways to study those things selectively if you want to understand them, and you can't really do that in an animal. But the opposite side of the coin is that a tissue culture is not the same thing as a living organism. If you really want to understand the overall biology, you need to go from *in vitro* models and study other parameters in animal models or in man."

"Some people would have the public believe that researchers use animals for the sake of using animals," says Pakes. "That's not true at all. When you have to have coordination and interaction among systems, then you obviously can't do it in a tissue culture system. You have to go to the whole animal."

Biomedical research has evolved to a point where actual experimentation is prefaced by review and justification. If using any living vertebrate, a UTHSCD investigator must submit a formal detailed proposal of the experiment for review. Human research goes through the Institutional Review Board. Proposals

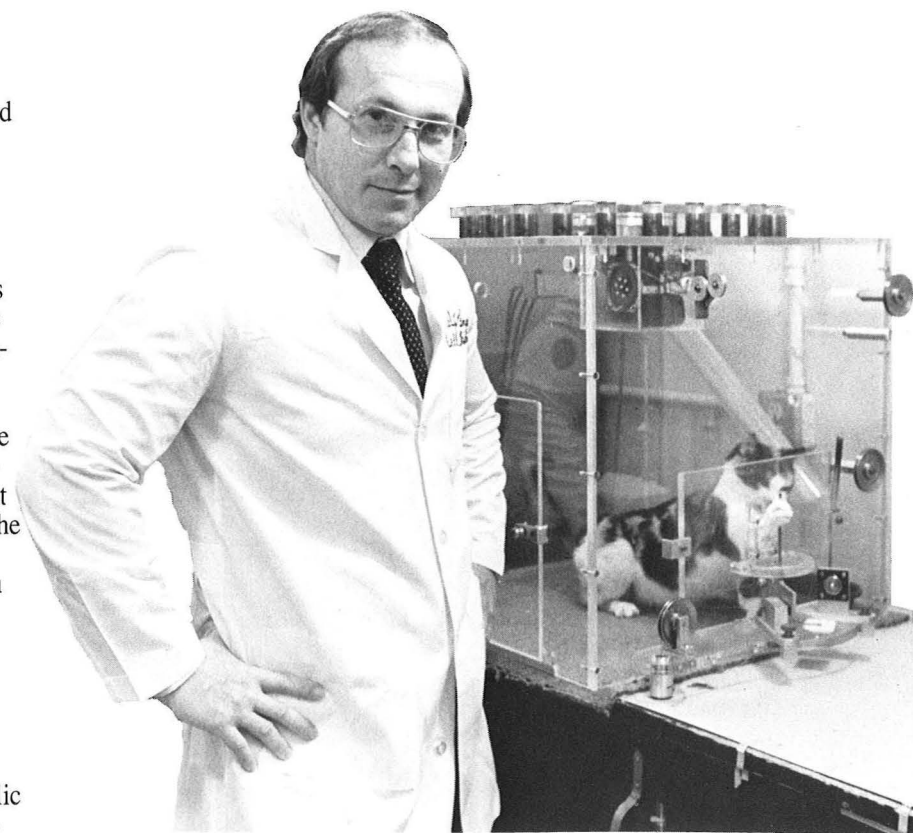
involving animals go to the Institutional Review Board for Animal Research (IRBAR). An investigator must go through the review process whether or not he is soliciting a grant from NIH or another funding agency.

The investigator must comply with standards set by the U.S. Department of Agriculture and the Public Health Service of the Department of Health and Human Services. A parent committee, the Institutional Animal Advisory Committee, oversees all aspects of animal use including housing and space requirements.

"The IRBAR reviews all animal use

greater detail and present them for discussion before the committee. Those are evaluated much more critically."

Each research project moves medical science closer to the goal of alleviating pain or sickness so that life may be more fully appreciated. It is that higher quality of life for which Haidet and the other researchers are working. Haidet refers to a bell curve for illustration of his studies on aging. "At twenty years, I start at the top of the curve. That's what my functional exercise capacity is. By the time I'm 70, my



William Gonyea, Ph.D., studies the process of muscle growth through weight-lifting cats.

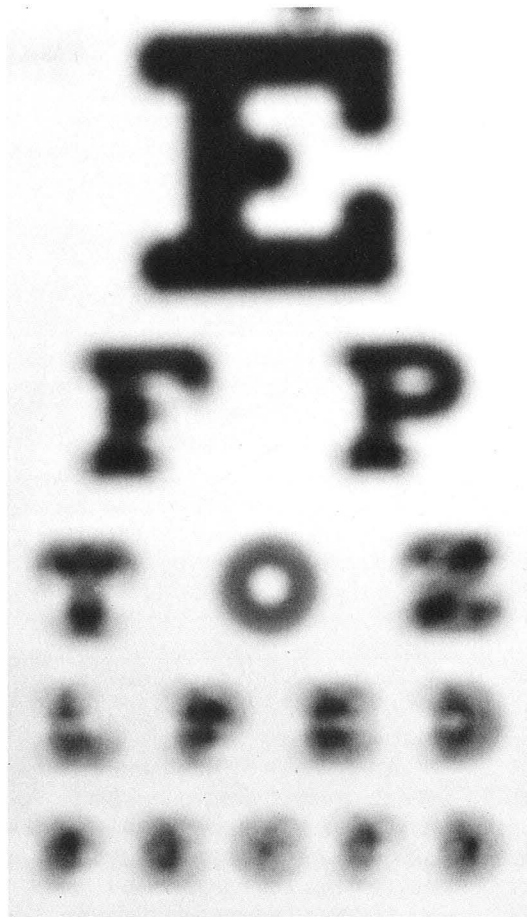
forms submitted. The appropriateness of the animal model proposed is just one of the many things the board considers when reviewing a protocol," explains Dr. Lauretta Gerrity, assistant professor of comparative medicine and cell biology and anatomy, and member of the IRBAR. "However, protocols involving survival surgery, or studies where animals may experience pain or distress, are assigned to a primary and secondary reviewer who go into them in much

exercise capacity is near the bottom of the curve. It may not be a straight line, but it goes down. If you attenuate that slope, you make it less steep. In the long run, the goal may not be so much to cause you to live longer; it may be to slow down the rate of decline, so that when you come to the end, you're not rolling off the edge in a wheelchair. You're running to the end—or at least, walking briskly." ■



# A LIVING LENS

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By Tommy Bosler



Patricia Lola had resigned herself to being blind in her left eye. She could distinguish light from dark, but that was all. An inflammation within her eye had led to a cataract, and the danger of subsequent inflammation made implanting a synthetic lens too risky. Ms. Lola had expected to wear a contact lens but found she couldn't tolerate one because her inner eyelid was badly scarred. Then she heard about a new kind of lens. One that didn't have to be taken out and cleaned. One that actually grew to the eye and became

part of it—became a “living lens.” She decided to try it, and a year later her corrected vision was 20/30.

The living lens is the result of a type of eye surgery called epikeratophakia, which translates roughly as a graft over the cornea. It is one of several types of keratorefractive surgery that change the shape of the cornea to help the eye focus more sharply.

Epikeratophakia is effective in correcting many of the same problems that can be helped by glasses or contact lenses: to correct nearsightedness (*myopia*) or farsightedness (*hyperopia*), to compensate for the loss of a lens through cataract surgery (*aphakia*) or to correct certain corneal deformities (*keratoconus* and *keratoglobus*). All of these problems cause light rays to focus poorly.

Light hitting a normal eye is bent by the clear cornea that covers the iris, bent again by the lens just behind the cornea and focused on the retina, the light-sensitive tissue in the back of the eye. The retina converts light impulses into nerve impulses, which are sent along the optic nerve to the brain, where “seeing” actually takes place.

If the light rays are not focused properly on the retina, the brain receives a blurred or distorted image. The cornea accomplishes about two thirds of the focusing and the lens one third. Defects in either the cornea or the lens are usually corrected by glasses or contact lenses. In the past, if glasses or contacts were ruled out, a corneal transplant offered hope in some cases. Now the possibility exists of correction through surgery less serious than a corneal transplant.

“Keratorefractive surgery is one of the most exciting developments in ophthalmology in decades,” said Dr. James P. McCulley, chairman of the Department of Ophthalmology at Southwestern Medical School. “It is going to change the practice of ophthalmology and have a major impact on the way visual defects are dealt with in the future.”

In the case of epikeratophakia, commonly called “epi,” the cornea is altered by grafting on a thin layer of donated corneal tissue, which becomes the living lens. The surgical technique was developed at Louisiana State University Eye Center in New Orleans in

1979 by Dr. Herbert Kaufman.

Dr. Mary Beth Moore, assistant professor of ophthalmology, did a post-residency fellowship there to learn the process and began performing it at the health science center in September 1985. During the first 18 months she did 25 surgical procedures as part of a nationwide study to evaluate the effectiveness of epikeratophakia. She is also training other UTHSCD ophthalmologists in the technique.

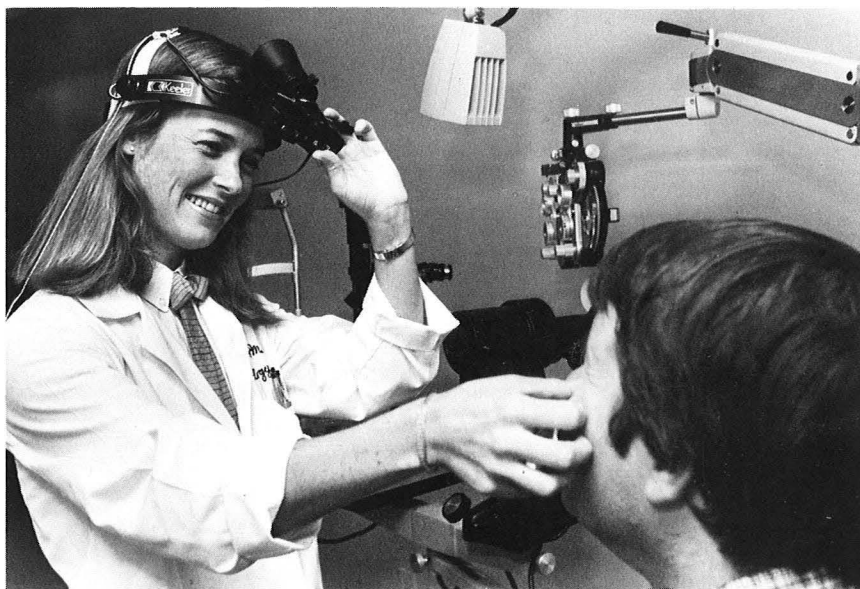
“Our success rate for the first year and a half was very good,” Moore said, “Only three patients did not adapt to the graft well. And one of the beauties of the epi is that it can be removed easily if it is not successful.”

The basic process for performing an epi is similar in correcting all types of refractive problems. Donated corneal tissue is spun in a centrifuge to remove its excess water and is frozen on a cryo-

lathe, a contact lens lathe that has been modified to cut corneal tissue. The frozen cornea is shaped according to the patient’s optical measurements. A computer makes the mathematical calculations and provides the settings for the cryolathe. This “living contact lens” is thawed and placed into a storage container.

In the spring of 1987, the health science center’s Transplant Resources and Services Center began providing corneal tissue for the grafts. Ellen Heck, administrative director of the center, explained that a donated cornea must be in almost perfect condition to use for a transplant but that less strict guidelines apply for graft tissue.

“We worked for almost a year perfecting the technique so that we could provide fresh tissue for patients,” said Heck. “Before that it came from a commercial source and was freeze



Mary Beth Moore, M.D., has good news for Mark Welch at a checkup 10 days after surgery. In 1985 Welch was the first patient to receive an epikeratophakia at the health science center.

**“It is going to  
have. . . a major impact  
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in the future.”**

James P. McCulley, M.D.

dried. Dr. Moore believes fresh tissue will offer a significant advantage to the patient by taking less time to heal and perform satisfactorily.”

At the time of surgery, the surgeon first prepares the patient’s cornea by gently wiping off the surface cells and making a shallow circular cut about the size of a hard contact lens. The edge of the living lens is placed gently into this cut and 16 stitches inserted to hold it there until it heals. The patient’s own



cells grow back over the graft within one week. The stitches are removed after several months.

The only place that the graft adheres to the recipient is at the site of the circular cut. For that reason, the operation is reversible. Should the graft need to be removed or replaced, the site of adhesion can be cracked and the graft lifted off with forceps.

The surgery is performed on an outpatient basis. The patient comes to the hospital early in the day. The procedure, which takes about an hour, is done in an operating room with the patient under general or local anesthesia. As soon as he is fully recovered from the anesthetic he can go home, usually in the early afternoon.

For the next five to seven days, until the eye heals, the patient must be checked frequently by the physician. Ointment or drops are put in the eye for about two or three weeks after surgery. During the early postoperative period, the eye is red and very sensitive to light. Until the stitches are removed, vision is blurry. It clears up gradually.

Patricia Lola's experience was typical. She went into surgery on December 30, 1985. She said, "Once I recovered from the anesthetic there was no problem with the eye's hurting or being painful. Of course, I wore an eye patch."

Lola did have one complication during her recovery, caused by the same scarring on her inner eyelid that had kept her from wearing a contact lens. "The scarred eyelid tended to rub off the new cells that were growing over the graft. I was really getting a little concerned at that point, but Dr. Moore put a very clear contact lens on my eye. I thought I wouldn't be able to wear it, but I wore it with no trouble at all and left it on for about two weeks. At the end of that time, the new cells had taken."

After Lola's cells had grown across the graft, Moore removed the stitches in two sessions, about a week apart. "Within two or three months I could distinguish shapes, but I didn't have good vision. My vision really began to pick up about nine months after surgery, and a year later it's 20/30 with my prescription."

A minor problem, from her point of view, was the number of times she had to go for follow-up examinations. She had

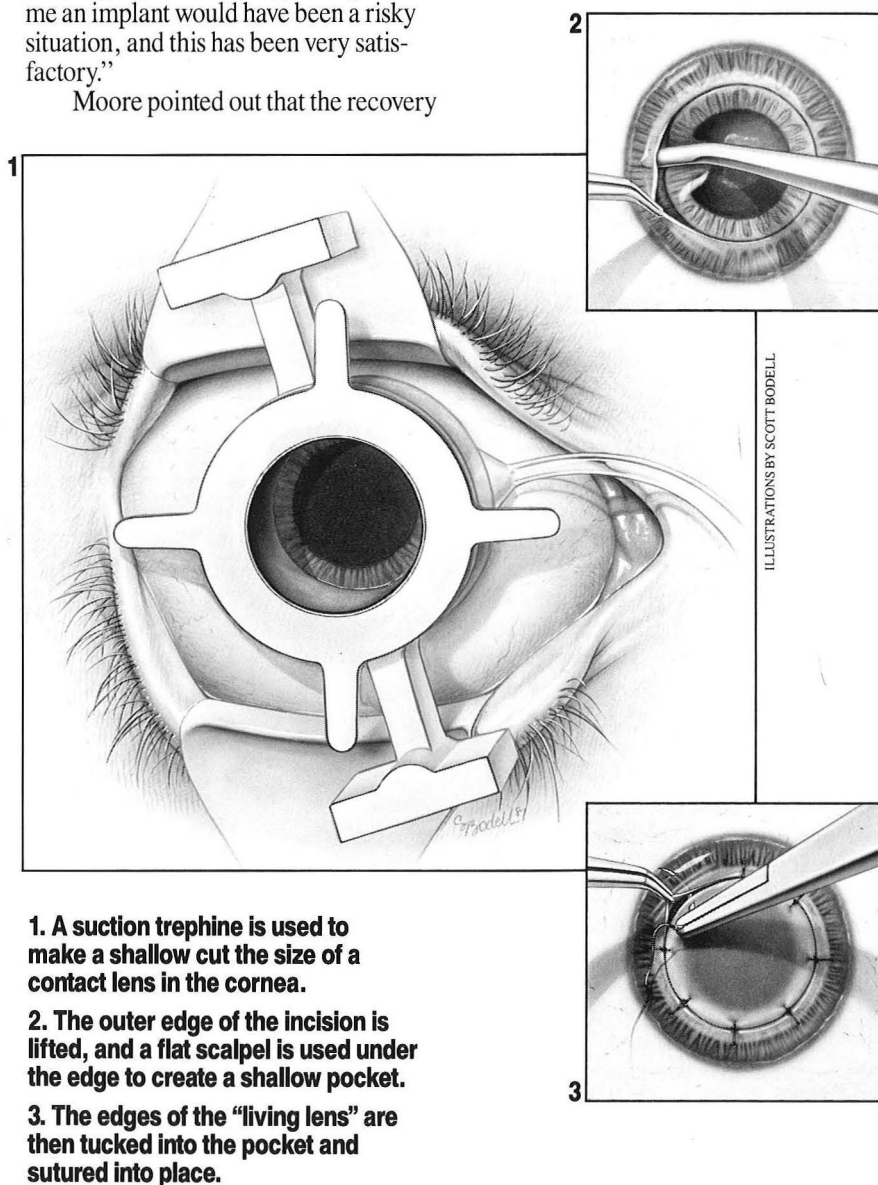
returned to her work as kindergarten coordinator at a private school in mid-January, only weeks after surgery, and found that juggling her work schedule and eye appointments wasn't always easy. "People do need to consider that and be able to make the time for it," she said.

Lola is glad she had the surgery and feels that she was well informed about what to expect. "I think anybody contemplating an epi needs to realize it is not an overnight situation, and Dr. Moore made that very clear. It is not like a lens implant, where I understand people get good vision right away. For me an implant would have been a risky situation, and this has been very satisfactory."

Moore pointed out that the recovery

period is not confining. "In the first place, we operate on one eye at a time so the patient does have the use of the other eye. Then, the actual time for the vision to become very clear depends to some extent on the problem that is being corrected. The myopic and keratoconus epis clear very rapidly, within the first one or two months. Aphakic epis in children clear very rapidly but in adults can take six months to a year to get to the final stage of clear vision.

"Meanwhile, the vision can be corrected with glasses if there is a particular need, but they might have to be changed



frequently as healing proceeds.”

Although the general procedure described above applies to all epis, there are some important differences in the way it is applied to the various refractive problems:

## APHAKIA

Cataract removal is usually followed immediately by the implant of a synthetic lens. In some cases, however, a synthetic lens is not recommended, and the person becomes aphakic.

Few surgeons, for example, will put an intraocular lens inside a child's eye. Children don't tolerate contact lenses very well, and they cannot wear thick cataract glasses on one eye and thin glasses over the normal eye. This would give them "lopsided" vision. Furthermore, if a child is less than six years old, the aphakic eye will become lazy and develop amblyopia because it cannot see clearly during a critical time of visual development. Epi benefits such children tremendously. In fact, their plight was the impetus for developing the procedure.

Adults who do not receive an intraocular lens at the time of cataract surgery usually wear a contact lens, but some cannot. The elderly may not have the hand coordination to insert and remove a lens. Some, like Patricia Lola, may not be able to wear a lens for other reasons. And younger adults who work in environments full of dust or dirt have difficulty wearing a lens. In all of these cases, epikeratophakia is a possible solution.

An epi compensates for the absence of a lens by adding extra curvature to the cornea. The graft is thick in the middle and thin on the edges.

## KERATOCONUS AND KERATOGLOBUS

Some patients who are nearsighted find that their myopia worsens progressively to the point that it cannot be corrected by their glasses or contact lenses. This occurs because their corneas have thinned and bulged forward. If the thinned area is only in the center of the cornea, the condition is called *keratoconus*; if it is thin all over, it is called *keratoglobus*.

Prior to the development of epikera-

trophakia, the only option for correcting thin corneas was corneal transplant surgery. Now an epi can thicken the cornea, allowing the patient to resume wearing eyeglasses or contact lenses. A flat graft, with no optical correction, is sewn tightly over the weak cornea, flattening it and pushing it back into place.

## MYOPIA

Some people need a more permanent solution to severe nearsightedness than eyeglasses or contact lenses. Perhaps their jobs require good eyesight without the use of corrective lenses or they have tried contact lenses and cannot wear them. There are two types of

keratorefractive surgery that have been tried for myopia: radial keratotomy and epikeratophakia.

Radial keratotomy is a process that was developed in Russia and has been practiced in the United States for about 10 years. This surgery involves making eight short slits inward from the edge of the cornea in a pattern like the spokes of a wheel. The incisions flatten the cornea and cause light to be focused farther back in the eye, closer to the retina.

The process is relatively simple, but some limitations were revealed by evaluations at leading medical centers around the country over a period of several years. First, radial keratotomy effectively corrects only low to moderate myopia (-2 to -6 diopters). Second, and more important according to Moore, the eventual success and degree of correction depends on the formation of scar tissue at the sites of the incisions, an element that varies between individuals and cannot be predicted. Finally, the procedure cannot be reversed. Nevertheless, it is an option for people with low degrees of myopia who for some reason connected with their jobs cannot wear glasses or contacts—airline pilots or workers in a dusty environment, for example.

For people with more severe myopia, an epi appears the better surgical alternative. The graft is concave in shape and therefore flattens the curvature of the cornea when sewn into place.

As effective as epikeratophakia is proving to be, Moore points out that there are some risks connected with the surgery. The correction obtained may not be completely adequate, and additional correction with glasses may be needed. As with any surgery, there could be possible complications from anesthesia, drug reactions or subsequent infection.

On the other hand, patients can experience permanent correction of severe problems—problems that cannot be corrected by glasses or contact lenses alone.

“For some people, epi will offer the only hope of normal vision. For others it is an innovative alternative,” said Moore. “But it's not just cosmetic surgery for the eyes—a way to avoid wearing eyeglasses. It is not to be undertaken lightly.” ■



**For Patricia Lola  
a synthetic  
lens implant would  
have been risky.  
Epikeratophakia was  
the answer.**



▼  
BY ANN  
HARRELL

# FILLING THE VOID

**"THERE IS NO I. THERE'S  
JUST AN IMMENSE HOLE AT THE CENTER.  
AN EMPTINESS. A TERROR.  
NOT ALL THE FOOD IN THE WORLD  
COULD FILL IT. BUT I TRY."**

**T**his was a cry for help from a woman in her 20s. It expresses an idea stated over and over by victims of bulimia, said Dr. David Waller, associate professor of psychiatry. Waller heads a major clinic for patients with anorexia nervosa, bulimia and related eating disorders at the health science center.

Because these eating disorders "span psychiatry and medicine," said Waller, the clinic employs a team approach, joining the disciplines of internal medicine, nutrition, dentistry and other related areas with psychiatry and psychology. At the same time, the team is searching for more knowledge about the causes and cures of eating disorders. It is this individualized approach to patient care coupled with a major health science center-based research effort that makes the UTHSCD program so successful.

The name bulimia, Waller said, is derived from the Greek words *bous*, which means ox, and *limos*, meaning hunger. The disorder is characterized by recurrent episodes of the compulsive eating of large quantities of food, especially carbohydrates. The episodes are often followed by self-induced vomiting, fasting or laxative abuse.



Depression or self-deprecating thoughts usually follow.

A young woman with bulimia is more difficult to identify than one with anorexia—and victims of both eating disorders are usually female. Because the anorectic woman may literally starve herself to death or bring on a heart attack by weakening her entire system, her plight is usually taken more seriously than the bingeing and purging behavior of the bulimic. Furthermore, a woman with anorexia may lose 20 to 30 percent of her body weight. Her appearance calls attention to the fact that something is dreadfully wrong, no matter how hard she tries to hide under baggy clothing.

The teenager or young woman with bulimia, on the other hand, may escape notice since she rarely loses a great deal of weight and in some cases may even retain her normal weight. However, this does not mean that her compulsion is not dangerous to her physical health, stressed Waller, or that her bingeing and purging behavior is not a call for help instead of a fad. Furthermore, national researchers report that bulimia is far more common than anorexia in the adult population.

Recently Marsha Mason, four-time Oscar nominee as best actress, made her TV-directing debut with a CBS special about bulimia in teenagers called "Little Miss Perfect." The show was about a "typical" high school girl, facing many different pressures in her life and trying to live up to her parents' expectations, who falls into the trap of bulimia. "It's so scary to read the research and interview all the young actors and actresses," Mason said. "I asked them if they knew anyone with bulimia, and without exception they all knew someone or had bulimia themselves. Young kids believe they can stop it any time they want."

Many people have the mistaken idea that bulimia is not dangerous. But team members who work daily with patients say this is not true. There can be severe disturbances of electrolyte balance, stomach ruptures, ulcers and major dental deterioration. In addition, there is always the danger of asphyxiation from vomiting, said Kathy Sedlet, nutritionist for the Eating Disorders Clinic.

The victim of bulimia also suffers from mental devastation. Dr. Bettie Hardy, team co-director and psycholo-

gist, plays an important role in the treatment of the bulimic patient. Patients are evaluated psychologically, and individual support programs are suggested to help them deal in a positive way with the problems in their lives.

Kim Chernin is a psychotherapist and author of *The Hungry Self*, a book about women and eating disorders that made the best-seller list. Chernin also finds that there is both immense physical and mental wreckage to young lives. She wrote, "...women involved in this troubled behavior often abandon their careers and their studies as the preoccupation with food takes over...they frequently return home, become extremely dependent on their parents...their growth and development as human beings virtually comes to an end."

There seems to be a prevalence of bulimia among two groups: teenagers who are trying to establish their own identities and college women who are stepping out into their own personal worlds for the first time. Chernin said that she has come to believe from her experience with women battling eating disorders—whether they are in their teens or are older—that they are experiencing an identity crisis. "When an eating disorder develops at what might otherwise be a turning point in a woman's life, this marshaling of resources for growth is not taking place. Instead of freedom and liberation we find obsession, and in it the underlying quest for identity and development is drowned," she wrote.

Hardy said that in some schools where the pressure for achievement is high it is not unusual for the bulimia rate to correspond. Parents' expectations, not just institutional ones, are also often involved in the kinds of pressures felt by the students who succumb to bulimia.

Metaphorically, their small bathroom may be offering these victims of bulimia a place to hide. Waller said that some of his patients report feeling like actors in a play, performing roles others have selected for them. Other clinic patients say that they often feel like they are wearing masks.

Chernin also gave examples of this kind of pretense in her book:

"On the day she was getting married she wouldn't come out of the room where she was dressing. It was

late. She wouldn't talk to anyone. Finally, they got me and sent me in there...I took one look at her. Red eyes, that certain look in them. I knew she'd been vomiting...She took a swig of toilet water—you know, to hide the smell? And what was the whole thing about? She didn't want to marry that guy. And she couldn't tell them. She was engaged for a whole year and a half. Always pretending. You know what I think?...I think it was her only way out. That vomiting is some kind of scream of anguish. I think she was using that vomiting to let them know there was really something she just couldn't stomach."

The bulimic patients Waller and psychologist Bettie Hardy see appear to have problems with certain kinds of pressure and also seem to use bingeing as a way of relieving themselves of anxiety. Soon they find that the bingeing-purging pattern can't be controlled.

"For people with this kind of problem," said Hardy, "stresses caused by new schools, new jobs or other major life changes seem particularly hard to deal with." The victim of bulimia often suffers from a deep sense of shame about her lack of control and attempts to hide her bingeing-purging pattern. As these activities become compulsive, the shame deepens and the behavior becomes even more secretive. Even after the bulimic patient is "cured," new stresses may lead to new episodes of bingeing and purging.

Although bingeing-purging behavior has always been noted in certain individuals in our culture, it is only in recent years that it has reached epidemic proportion. And there seem to be certain "mini-cultures" in which it thrives. Certainly, today's preoccupations with sylph-like bodies set the stage in the college years. These are compounded by the pressures young women face in attempting "to have it all"—find the perfect mate, launch a brilliant career and raise perfect children.

In 1983 *Ms.* magazine reported that at least one-half of college coeds at that time showed evidence of eating disorders. According to the report by Michael G. Thompson, Ph.D, and Donald M. Schwartz, Ph.D, "The most dramatic finding was the prevalence of anorexic-like behaviors among



normally functioning college women. These women were not impaired in their work, though they often felt that they were struggling."

Equally frightening is Chernin's belief that teens and young women are teaching each other how to lose weight by ritual bingeing and then purging. Freshmen begin to emulate upperclassmen in their choices of diet colas and salad bars—and many are initiated into the secret ritual of vomiting and purging with laxatives. But no one tells them that this shared method of control will soon be controlling them.

Dr. Rekha Pole, assistant professor of psychiatry and member of the UTHSCD clinic team, has analyzed the relationship between victims of bulimia and their parents. Studies suggest that, while the parents of a child with the disorder may be excellent parents in many ways, there may be something lacking in the relationship. This missing ingredient, according to these studies, is empathy—a sense of understanding on the parents' part of what it is like to be the child and of caring deeply about the daily battles the child goes through.

Empathy is a special kind of care that helps children develop a sense of self and a way of "soothing themselves" when they are depressed or troubled, things that are important in adulthood, said Waller. Perhaps, he speculated, food in some cases becomes an extreme substitute for this ability to comfort or soothe oneself.

Pole has found that children raised with too little empathy and too much control have a developmental defect and may not develop an internalized sense of self. Often when this "empathy defect" is suspected in a clinic patient's background, a special type of psychotherapy, one that tries to help the person to comfort herself in times of crisis, is introduced to the patient.

Lack of selfhood is another problem that may also be attacked with psychotherapy. One patient, Waller related, felt like she was two different people: one at home and another at work. She needed to learn to integrate and become her own self, not what others wanted her to be, he said.

Researchers in the Department of Psychiatry at the health science center are also beginning to view bulimia as a

problem of food abuse, in the same way that psychiatrists regard alcohol abuse or drug abuse. In fact, victims of bulimia have several psychological features in common with alcohol and drug abusers, said Waller. People suffering from bulimia actually become addicted to their bingeing-purging behavior. "They simply cannot become abstinent," he said.

Purging becomes necessary, continued the psychiatrist, because terrible feelings come with the binges, the patient's individual concerns become heightened and there is a buildup of anxiety. "The rewards come with the binge: there is a reduction of anxiety, the memory of hunger disappears and any depressed feelings experienced by the patient are gone."

Like a drug or alcohol addict, patients who have been "cured" may have a setback in their lives and go back

**P** EOPLE SUFFERING  
FROM BULIMIA  
ACTUALLY BECOME  
ADDICTED TO THEIR  
BINGING-PURGING BEHAVIOR.  
THEY SIMPLY CANNOT BECOME  
ABSTINENT. *David Waller, M.D.*

to their addictive behavior—over and over. In addition, studies have shown that the most difficult times to resist their cravings are the unstructured times in their lives. Sundays, especially Sunday evenings, are especially difficult for the addict, Waller commented. "Many patients report a feeling of 'psychological emptiness' then."

Researchers in the laboratories at the health science center are also looking for answers to the problems of eating disorders. They think the answer may lie with some neuropeptides that modulate signal activity between cells in the brain and other organs. In particular, endogenous opioid peptides, which have actions similar to drugs like opium or morphine, have been discovered in the brain as well as other parts of the body. It is thought that they play an important role in pain pathways and altering the response to stress.

Although anorectic women are literally starving themselves to death, they do not seem to feel hunger pains, cramping and other disorders caused by their self-starvation, Waller said. It is thought that their beta endorphins, an endogenous opioid, may be involved in the perception of pain and even cause a euphoric feeling like the "runners' high" reported by some athletes.

Other researchers have found evidence of elevated levels of endogenous opioid peptides in the spinal fluid of patients with anorexia, leading to the speculation that anorectics may produce more opioids than people who do not suffer from this condition. However, it has not been determined whether the increased opioid peptide production was caused by the patient's anorectic condition or whether it was a consequence of major weight loss.

Similar tests using blood plasma were set up by the UTHSCD researchers to look at beta endorphin activity in bulimic patients by analyzing their blood plasma rather than subjecting patients and volunteers to a painful spinal procedure. They were also interested in pursuing this line of study because related animal studies with plasma have linked opioid peptides to eating behavior.

Waller and his research team decided to study normal-weight bulimics so that there would be no chance that any changes in endorphin levels could be linked to weight loss. Normal-weight controls, who were not depressed and were from the same socio-economic group as the patients, were selected. Besides investigating whether the level of plasma beta-endorphin activity is altered in bulimic patients, the study asked whether any such alteration might be related to the severity of their abnormal eating attitudes and behaviors or to depression. Researchers also looked at whether depression ensued with a change in beta-endorphin levels.

Results of the study showed a clear relationship between low levels of beta endorphins and behavior—that is, a preoccupation with food. However, it is not clear whether the low levels of beta endorphins are caused by the bingeing and purging behavior or whether this behavior is brought on by the low levels of beta endorphins in the blood. The

beta endorphin level did not relate to depression.

Waller said that, while drugs that "block," or prevent, the endorphins' connecting with their receptors in the brain have been found to help some anorectic patients, much less is known about the treatment of bulimics. However, pilot studies are going on in which anti-opioids, or opioid antagonists, are being given to bulimic patients. Also, some bulimic patients, both with and without signs of depression, are being tried on anti-depressant drugs.

Clinic researchers, in addition, are collaborating with scientists in the psychiatry sleep center on studies looking at the relationship of bulimia and deviations from normal sleep patterns.

Furthermore, in support of the idea that bulimia is a problem of food abuse, plasma studies in humans done here and elsewhere have suggested a relationship between beta endorphins and glucose regulation. The relationship indicates that the abnormalities in beta-endorphin regulation of eating may be connected with the addictive behavior of patients with eating disorders.

Dr. Ingbert Fuchs, UTHSCD psychiatry faculty member, is involved in conducting other studies that researchers hope will give clues for the development of drugs to treat bulimia. Fuchs is doing studies in which rats are put on restrictive diets consisting of only protein or fats or carbohydrates, the latter being the major food bulimics seem to crave. The rats are then studied to see what changes in peptides have occurred in their brains while on these diets.

The researcher is also interested in seeing if major diet restrictions can change the animals' food preferences. Waller said that studies by other researchers have previously indicated that rats given unlimited amounts of rat food will limit their own diets while rats offered unlimited amounts of sugary pastries will soon balloon into fat rats.

Together the clinic team and its consultants search for the causes of this little understood condition as well as for clues to its cure. "The answers have to be biologic," said Waller, "because the brain and its related system is where the mind is." ■







ILLUSTRATION BY RANDY PADORR-BLACK

**O**n June 23 ground was broken for University Medical Center, a private 159-bed teaching and referral hospital affiliated with The University of Texas Health Science Center at Dallas and Parkland Memorial Hospital.

Although a referral hospital has perennially been at the top of the administration's strategic planning lists, there were legal and economic hurdles that made its realization unlikely. The fact that the University Medical Center

is under construction and expected to open in early 1990 is due solely to a handful of civic leaders who faced each hurdle as an entrepreneurial challenge.

## Hurdle 1

*A Texas policy that prohibits use of state funds to build or operate new university hospitals*

"We'd been talking about the hospital since I came here," said Dr. Charles Sprague, president of UTHSCD from 1967 until 1986. "Tom Shires, who chaired surgery when I came here, made it clear that at some point we needed to have a university hospital." Dr. Shires made his point by leaving Southwestern

for the University of Washington Medical School, which promised a referral facility, and taking most of the surgery faculty with him.

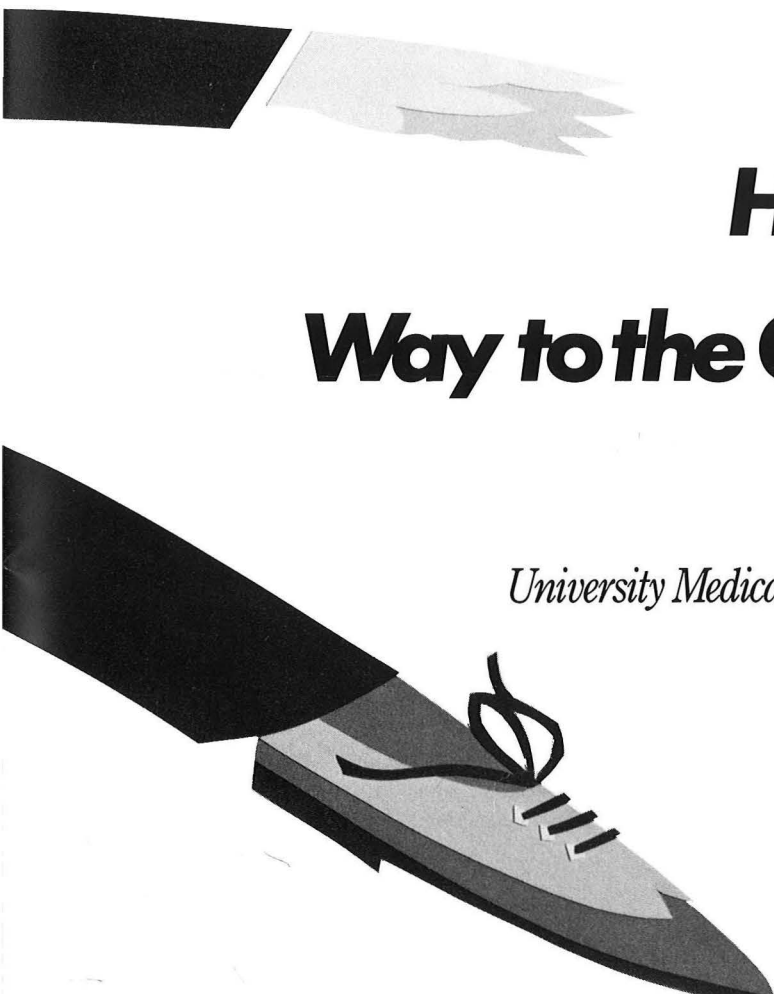
Sprague explained, "Of course, the university could not provide a hospital, and the state could not provide it, so we looked at various other ways."

Those ways included special working relationships with private hospitals. For example, the Department of Surgery once had offices at Presbyterian Hospital. But such relationships proved logistically impossible.

The idea of asking a proprietary hospital corporation to build the hospital as a showplace was considered. That idea was rejected because the corporation would ultimately have to show a profit to its stockholders, possibly at the expense of the health science center's interests.

"It was something we wanted and expressed a need for, but I very honestly didn't know how it was going to come about. It was just a fortuitous circumstance that private support came along at the time it did," said Sprague. Considering the circumstances, *fortuitous* is an understatement.

One December evening in 1981 Dr. Robert Kramer and his wife were having dinner with their friends Bruce and



# A Funny Thing ..... Happened on the ..... Way to the Groundbreaking

.....  
**By Tommy Bosler**  
.....

*University Medical Center could have stumbled at the hurdles  
without high-stepping civic support.*

Lynn Lipshy, Kramer is a clinical professor of pediatrics and director of the Cystic Fibrosis Treatment Center at Children's Medical Center. When conversation turned to the medical school, Lipshy said that the Zale Foundation had supported various projects at the school over the years but he wondered what the medical community in Dallas really needed.

Kramer suggested a hospital at the school where the faculty could hospitalize referred private patients. He said he believed that other medical specialties deserve the type of referral facility that Children's Medical Center offers the pediatrics faculty.

"That was one of the most selfless acts of my career because the University Medical Center will exclude pediatrics," Kramer said at the groundbreaking.

Lipshy and Kramer did some quick mental calculations about the possible

cost of a 200-bed hospital at 1981 prices and came up with a figure in the range of \$37.5 million. "Let's do it!" said Lipshy.

He contacted his cousin Donald Zale, who was equally enthusiastic about the idea. In January 1982 Lipshy and Zale arranged a dinner at the Anatole Hotel to discuss the idea with Drs. Sprague, Kramer and Kern Wildenthal, then dean of Southwestern Medical School. Wildenthal and Sprague explained the need for a university hospital to the two men. That was the first of a series of discussions that also included Ben Lipshy, chairman and co-founder of the Zale Corporation. The discussions continued for almost a year, culminating in a request from the medical school to the Zale Foundation to fund a feasibility study.

## Hurdle 2

### ..... The Feasibility Study

One might wonder why a feasibility study was necessary when almost everyone agreed that the school needed a hospital for referred patients, but at the time the State of Texas' Health Facilities Commission had to approve each proposed new hospital or expansion. Without the commission's approval, no University Medical Center could be built, even with private funds. Unfortunately, it was a time of expansion for Dallas hospitals, and the commission could be depended on to scrutinize any further requests.

A steering committee was appointed to select the firm to perform the official feasibility study. Ben Lipshy chaired the committee, whose members were Sprague, Kramer, Dr. Al Roberts, Dr. Michael Romaine, president of the Zale Foundation, and Ralph Rogers, chairman of the board of Texas Industries and an active philanthropic fund-raiser. The committee received bids from 13 companies to do the



feasibility study, and they selected Robert Douglass Associates of Houston. The half-million dollars or so for the study was provided by the Zale Foundation, channelled through Rogers' community foundation, the Foundation for Health Education Research.

The study had several phases. Douglass Associates first assessed the need of the faculty for this kind of referral facility. One of the things they learned was that lack of such a hospital was holding back Dallas' growth as a referral center. Only 30 percent of Dallas hospital patients come from outside Dallas County. In Houston, 60 percent come from outside Harris County.

Then they studied the means by which such hospital beds could be provided: a wing at Parkland, some accommodations at St. Paul's or other ways. They concluded that a free-standing non-profit corporation should be formed to own and operate a hospital at arm's length from the medical school and Parkland but closely linked with both.

Once the feasibility study was complete, a non-profit corporation was formed as suggested—University Medical Center Inc. Sprague said, "Ben Lipshy and I tried to identify people who might serve on the board so we went around and invited people. The response surprised me totally because we went to some of the most prominent people in the city. Of the first dozen we went to, not a single one turned us down. It was very impressive—the kind of support we found early on in the community to meet this need."

The original board of directors included Ben Lipshy, Ralph Rogers, Paul M. Bass Jr., Charles G. Cullum, Lee Fikes, Gerald W. Fronterhouse, Richard F. Reynolds, Jere W. Thompson, Donald Zale, Mrs. Eugene McDermott and Peter O'Donnell Jr. Many of the same people pledged financial support.

In April 1984 the Board of Directors of UMC Inc. began working to secure the certificate of need required by the State of Texas, and fund raising continued. The Southwestern Medical Foundation adopted a resolution to support UMC although some private practitioners in the community had

reservations about the project.

Preparing the official certificate of need was a time-consuming process. Mike Romaine, president of the Zale Foundation recalled, "Ben Lipshy asked from the beginning if I would take this on as a special project and be the staff person to be sure everything was done—running around town, carrying paper, getting signatures, making sure the lawyers did this, that and the other. Since the Zale Foundation had pledged most of its assets to the project—almost \$9 million at that point—I had the time to do it."

Finally, in October 1984, University Medical Center Inc. held a press conference to announce that a certificate

*"The response surprised me totally because we went to some of the most prominent people in the city. Of the first dozen we went to, not a single one turned us down."*

*Charles Sprague, M.D.*

of need, supported by the Robert A. Douglass Associates' feasibility study, was being filed with the Texas Health Facilities Commission. By April 1985 the commission's staff appeared satisfied with the application, and a hearing was set for June.

In anticipation of receiving the certificate and beginning a public fund-raising campaign, the UMC Board of Directors elected Mike Romaine president of University Medical Center Inc.

But a funny thing happened.

In May the state legislature refused to grant the Health Facilities Commission a budget for the following year. Instead of working through the end of August, the time at which the Sunset

Law would go into effect, the Commission members simply packed up and went home. UMC's Certificate of Need was never granted, nor was it legally necessary after August 31.

## Hurdle 3

### *Fundraising in a declining economy*

"That summer was sort of a hiatus," said Mike Romaine. "We said, come fall we'll hire an architect and start raising funds in earnest."

The first task was handed to a building committee headed by two seasoned professionals: Dr. Philip O'Bryan Montgomery, a professor of pathology who had coordinated the expansion of the health science center's facilities and had been called in as coordinator of Dallas' downtown Arts District when the project appeared mired in dissension. William E. Cooper had helped the Dallas Market Center grow from 248,000 square feet to 10 million square feet in his 25 years as chief executive officer, a period of almost continual construction. Their job proceeded smoothly.

The fund raising, however, ran into a very high hurdle indeed—an economy in which oil had declined disastrously and in which real estate and electronics were beginning to slide. It was not a time to begin a public campaign.

The board of directors of UMC Inc. began exploring the possibility of a bond issue. Romaine explained that there were various ways they could have sought bonds. For example, they could have issued bonds themselves or have tried a public bond issue. However, they preferred the idea of getting a letter of credit from a local bank to get money from one of several bond pools in the state designed to fund health facilities.

They were exploring the latter possibility when tragedy struck. In November 1985 Ben Lipshy died within hours of having a heart attack. The project's leader and main fund-raiser was taken without warning. His son Bruce, a natural choice as successor in the UMC effort, was soon embroiled in a Canadian firm's hostile attempt to take over the Zale Corporation.

Rogers, whose physician had

*Continued on page 32*

# University Medical Center

Dallas' own University Medical Center was one step closer to reality on June 23 when ground was broken for the private 159-bed teaching and referral hospital affiliated with The University of Texas Health Science Center at Dallas and Parkland Memorial Hospital.

University Medical Center Inc., a private non-profit corporation organized in 1984 to develop the hospital, will operate the facility in a three-member consortium with the health science center and the Dallas County Hospital District.

University Medical Center will be the facility in which the medical school faculty can provide care for patients referred to them by other physicians. It will also provide more unusual and highly specialized cases for medical students to observe as part of their education. Parkland Memorial Hospital, the health science center's major teaching hospital, is devoted primarily to indigent and emergency patients from Dallas County.

University Medical Center will be completed in early 1990. Constructing and equipping the 264,000-square-foot hospital is budgeted to cost \$40.2 million. The hospital will have nine stories—a basement and levels one through eight above ground.

The ground floor, level one, will house the public and administrative areas while the basement level includes space for support services, as well as radiology services and a pharmacy.

The second level will contain six oversized operating rooms to accommodate special equipment needed for eye, ear, nose and throat surgery, plastic surgery, oral surgery, gynecologic surgery, urology, neurosurgery, orthopedic surgery, chest and vascular surgery and special general surgery. Two suites will be provided for outpatient surgery, in addition to specialized facilities for cystoscopy and angiography. The second level will also contain recovery rooms and a waiting room for family and friends.

The third level is designed to house 20 intensive care beds—12 for surgical patients and eight for medical patients, with a nursing station for each section. A large waiting room for the families of patients in the intensive care unit will open onto an outdoor deck at the front of the building. In addition, the hospital's medical laboratory and respiratory therapy facilities will be on this level.

Accommodations for psychiatry patients will be located on level four.

They consist of private rooms for 21 patients and generous space for group activities, including occupational and recreational therapy.

Levels five through eight contain private rooms for surgical and medical patients, approximately 30 to a floor. Each room has a private bath, and the design includes a built-in lounge-sleeper for the convenience of family members who might choose to spend the night. Many rooms have windows angled to provide a view of the downtown skyline. The patient-care floors also contain special treatment rooms and physicians' conference rooms to support the hospital's teaching role.

Because of its proximity to Parkland Memorial Hospital and Children's Medical Center, University Medical Center will not provide emergency, maternity or pediatric care. Parkland Memorial Hospital will provide some support services to UMC.

Offices and laboratories for faculty physicians whose patients are hospitalized at UMC, as well as additional classrooms, will be provided in the health science center's new Charles C. Sprague Clinical Sciences Building, which will adjoin Parkland and University Medical Center.

The architects of University Medical Center are The Oglesby Group of Dallas and Page Southerland Page of Austin. ■



already warned him against his level of activity, agreed to take over as chairman of the board until the bond issue was settled.

Meanwhile, the Building Committee's task was moving along admirably, having selected architects and moved to the consideration of preliminary plans. A formal search for a full-time president and chief executive officer for the hospital resulted in the hiring of Bruce Satzger in September 1986. Romaine, who had been the volunteer president for almost a year and a half, handed over operations to Satzger but remained active on several committees.

Romaine recalled, "Our financing struggle sort of bogged down when Ben Lipshy died. Ralph Rogers continued working on the letter of credit, but that didn't seem to work. He decided to go for a public bond issue."

Sprague said, "Looking back, it is very clear that financing would not have come about without Mr. Rogers. No way it would have happened. It was his idea to go to Dillon, Read & Co. Inc., and it was unbelievable the way that developed."

Under Rogers' leadership, UMC went to Wall Street in January 1987. Their proposal for financing was unusual. Rogers proposed that Dillon, Read sell tax-free revenue bonds for a private, non-profit organization to build a hospital that was a start-up project with no financial or operating history.

"We convinced Dillon, Read that the consortium of the health science center, Parkland Memorial Hospital and University Medical Center would work," said Rogers.

The process was a tribute to the strength of the contractual consortium between The University of Texas System, represented by its health science center at Dallas, the Dallas County Hospital District, represented by Parkland Memorial Hospital, and the University Medical Center group.

Each of the entities will provide certain benefits to the hospital: the health science center will provide medical staff; Parkland will provide contract

management and certain support services; and the UMC board will maintain policy and financial responsibility. That each of the entities would also reap benefits from the joint effort was elemental to its conception.

"Putting these entities together in a contractual consortium," said Rogers, "was quite a feat." It is a feat for which many people also credit Rogers.

On March 25, 1987, University Medical Center Inc. closed on a \$40 million tax-exempt bond offering, and the last major hurdle was overcome.

## Heading for the Final Lap

After the bond issue was settled, Rogers retired as planned. In April the UMC board elected Donald Zale chairman. In June ground was broken for the hospital and construction begun. But the race isn't over yet.

The campaign to raise funds to build the hospital will continue. Approximately \$23 million has been raised privately. The board hopes to

raise another \$15 million. UMC Chairman Donald Zale explained, "Because of the bond issue we have the money to begin construction now and see us through the initial period of operations, but that money will eventually be paid back out of earnings. Every cent that we receive from private sources means that earnings can be put into building new programs and keeping UMC state-of-the-art. That is, after all, the whole purpose of this non-profit corporation."

Bruce Lipshy, chairman of the fund-raising committee, said, "In the Southwest right now, everyone who's trying to raise money is having a hard time, not just University Medical Center.

"But there are lots of great people in Dallas who are very giving to the community, and lots of corporations and philanthropists. Our job is to explain to them why this project is so important to Dallas. I think we have a great story to tell. It just takes time to tell it to a lot of people."

The new team is in place and running. They'll reach the finish line in 1990. ■



*Ground breaking culminated six years of working and hoping for UTHSCD President Emeritus Charles Sprague, Bruce Lipshy and Robert Kramer, M.D. (from left).*

PHOTO BY T. RANDALL BLACK



# Vital Signs

## New relief for back pain

A procedure for treating painful, herniated disks of the spine without extensive surgery has proven safe in clinical trials and is now used within the medical community, says Dr. Vert Mooney, professor and chairman of the Division of Orthopedic Surgery.

The technique, which Mooney helped pioneer, employs an automated needle-like probe that cuts away and removes disk material pressing against nerves.

A herniated disk can cause severe back and leg pain when its rubbery nucleus bulges out and presses against spinal nerves. The feeling is often a burning, shooting pain down one or both legs called sciatica, because pain radiates down the sciatic nerve.

"We have been in real need of a safe procedure that can alleviate back and leg pain caused by a disk without the use of extensive surgery," says Mooney, adding that he has been encouraged by the success of this procedure.

Mooney uses the disk removal technique, called a percutaneous lumbar discectomy with aspiration probe, on selected patients. Specifically, the procedure has been found effective in patients who have a bulging disk that has not ruptured and spilled its contents into the spinal canal. In cases where rupture occurs, the more extensive laminectomy procedure remains the operation of choice.

In the discectomy procedure, the surgeon inserts the instrument through the skin alongside the spine. He is guided by both special X-ray equipment, which projects an image on a TV screen, and by the patient, who is sedated but not asleep and can tell the doctor if the probe has touched a nerve.

Following surgery, the patient



*Vert Mooney, M.D., with aspiration probe.*

spends only one or two nights in the hospital. This compares to an average hospital stay of a week after laminectomy.

Mooney says his health science center team was among the first groups in the country involved in clinical trials using the aspiration probe. Initial research on the procedure was performed in 1985 by a medical team at the University of California, San Francisco. To date, about 2,000 patients have been treated with the discectomy procedure nationwide.

While the discectomy procedure is relatively new, both the equipment and the approach have been used successfully for other purposes. The new procedure is preferable to disk-dissolving techniques introduced in the '70s that employed enzymes—techniques now considered too risky to use. ■ S.R.

## Ulcer personality not a myth

You have probably heard that there are two kinds of people—those who get ulcers and those who give them. Actually, peptic ulcers affect one in every 10 American men and one in every 25 American women sometime during their lives.

Peptic ulcers are holes or defects in the stomach lining or in the upper small intestine. The primary symptom is a burning, gnawing pain, sometimes resembling a "hunger pain." Ulcer complications, such as bleeding, perforations and obstructions of the intestinal tract, frequently lead to surgery and can be fatal.

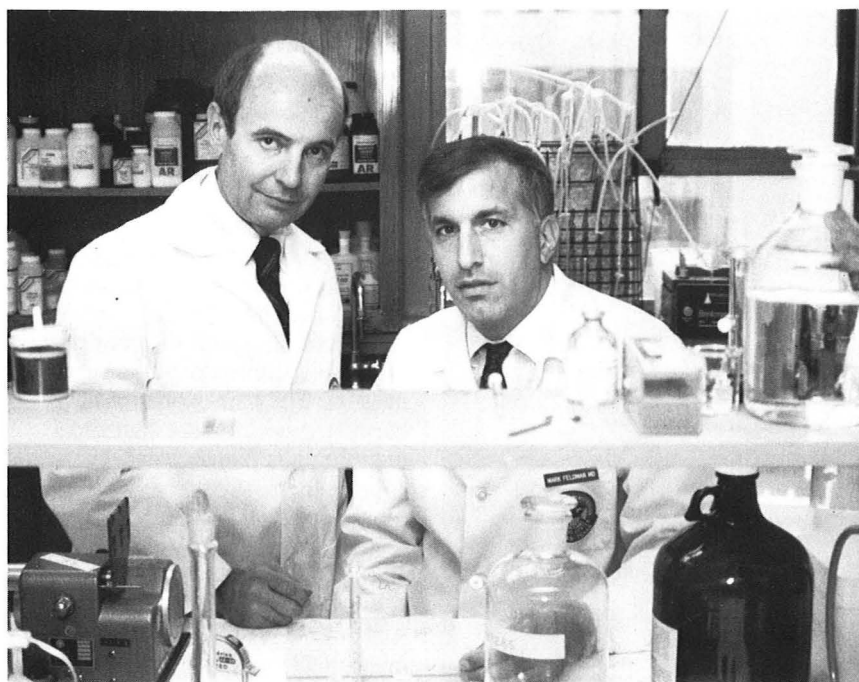
Gastroenterologists Drs. Charles Richardson and Mark Feldman, who jointly hold the Patterson Professorship in Internal Medicine, have studied a number of factors contributing to the cause of ulcer disease and have evaluated new methods of treating ulcer patients.

Working with patients at the Dallas Veterans Administration Medical Center, Feldman has found that personality plays a big part in whether peptic ulcers develop or not. In fact, he has identified psychological disturbances in patients who develop peptic ulcers and has also identified a set of behavioral risk factors that correspond with peptic ulcer disease.

Feldman, aided by clinical psychologist Dr. Pamela Walker, found that the dominant personality disorder in the ulcer patient volunteers was hypochondriasis. The patients tended to be pessimistic complainers who were preoccupied with their own aches and pains. While ulcer patients experienced the same number of potentially stressful life events as normal subjects, the ulcer patients perceived the events as having a far more negative impact on their lives.

Ironically, Feldman found that

# Vital Signs



*Charles Richardson, M.D., left, and Mark Feldman, M.D., have spent 11 years at the Dallas Veterans Administration Medical Center researching the causes and treatment of peptic ulcers.*

ulcer patients were more dependent on others yet had less social support than non-ulcer patients. The ulcer patients also suffered more anxiety and depression than the normal research volunteers.

Some patterns of behavior that Feldman saw in ulcer patients were excessive use of tobacco, alcohol or aspirin. The most serious of these was cigarette smoking, which delays ulcer healing. Death from peptic ulcer disease is more likely among patients who smoke.

Collaborating with Richardson, Feldman discovered that a chief factor separating ulcer patients from normal persons is a profound overproduction of stomach acid. Some ulcer patients secrete twice as much acid into the stomach over a 24-hour period as the average person, and higher amounts are secreted even while sleeping. The rea-

sons for overproduction of acid largely remain a mystery.

Peptic ulcer disease is probably caused by several factors acting in combination, the two doctors say. For example, increased acid secretion and emotional stress may be important mechanisms leading to ulcer formation in some patients while smoking or ingestion of drugs such as aspirin may play a major role in others. Genetic predisposition may be a factor in ulcer formation in certain "ulcer families."

There are other ulcer patients with no known risk factor or explanation for ulcer disease. In these patients some presently unknown mechanism or mechanisms presumably cause ulcers. With further research, the researchers hope additional causes of ulcer disease will be discovered and ultimately a cure will be available. ■ S.R.

## Double-barrelled treatment takes aim at LDL cholesterol

Researchers scored a bull's-eye in the treatment of moderately high cholesterol with a combined-drug therapy that lowered cholesterol-carrying LDL by 48 percent.

Patients with cholesterol levels in the range of 250 to 350 milligram per deciliters benefited from a double-barrelled treatment with two cholesterol lowering drugs—Lovastatin and Colestipol. Each of the drugs takes aim at a different mechanism for ridding the bloodstream of low density lipoproteins (LDL), the cholesterol-transporting particles that clog arteries, cause atherosclerosis and lead to heart attacks.

Lovastatin (formerly called Mevinolin) inhibits the production of cholesterol within cells, forcing the cells to pull the cholesterol they need from LDL particles circulating in the bloodstream. Nobel laureates Joseph Goldstein and Michael Brown of the health science center faculty were instrumental in describing the mechanism that causes a cell to turn on or off its production of cholesterol.

Colestipol is a gritty polymer or resin that attracts and binds bile acids, which have a cholesterol component. Since Colestipol cannot be absorbed by the intestines, it is excreted from the body.

Dr. Scott M. Grundy, director of the Center for Human Nutrition at UTHSCD, and Dr. Gloria-Lena Vega, an instructor of biochemistry, treated 10 patients whose cholesterol levels were in the 250 to 350 mg/dL range. They chose patients at the Dallas Veterans Administration Medical Center who had no apparent genetic cause, such as familial hypercholesterolemia, for their elevated

cholesterol levels.

Each patient received 20 milligrams of Lovastatin and 10 grams of Colestipol twice daily. The treatments resulted in a 36 percent decrease in total serum cholesterol, a 48 percent decrease in LDL cholesterol and a 17 percent increase in HDL cholesterol, the "good" high density lipoprotein that indicates cholesterol is being eliminated.

About 15 percent of all middle-aged Americans and 35 percent of patients with coronary heart disease have cholesterol levels exceeding 245 mg/dL. Most of these have primary moderate hypercholesterolemia like the group in the study.

Grundy says that a maximum effort to lower LDL with medication is not necessary for everyone in the moderate category. "Careful attention to diet, sometimes combined with one drug, is often able to bring cholesterol within a safe range.

"However, we think the two-drug treatment is appropriate in certain high-risk cases. For example, persons who have undergone coronary bypass surgery and who have moderately elevated cholesterol levels may develop new blockage in their grafts and in other arteries. Another group is cigarette smokers who have hypercholesterolemia. Their risk for coronary heart disease is six to 10 times the average.

"Moderately high cholesterol combined with high triglycerides puts a person in a high-risk category that could benefit from this treatment. It also shows promise for reducing the chance of atherosclerosis in non-insulin-dependent diabetics, but we need to do more testing in this category."

On Sept. 1 the Food and Drug Administration approved Lovastatin for use in the United States. It will be sold by Merck Sharp & Dohme under the trade name Mevacor. ■ T.B.

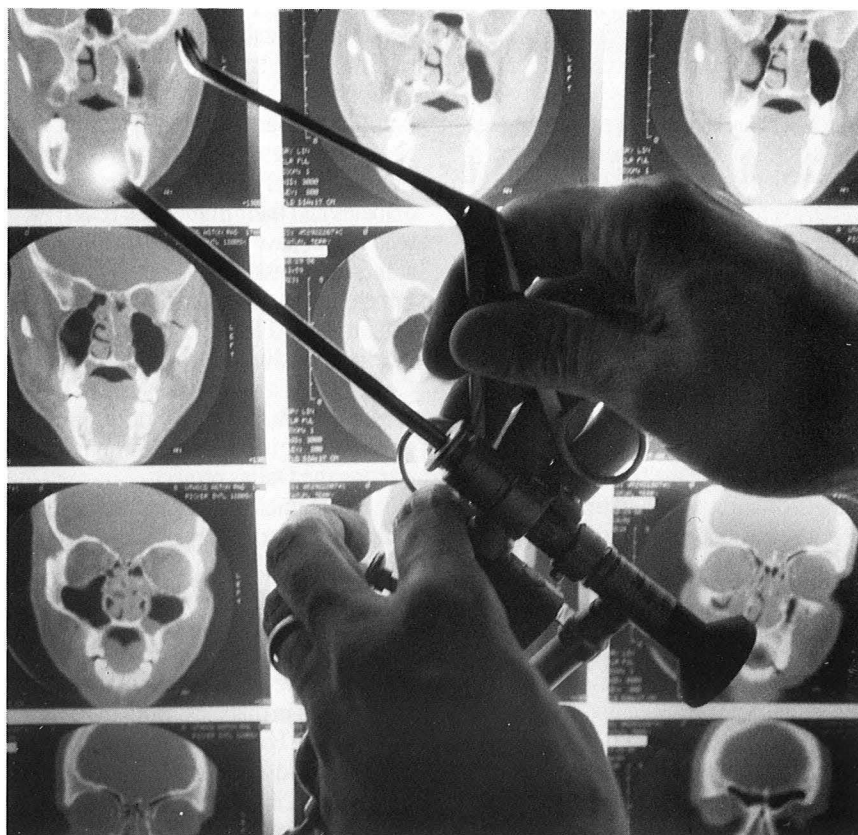
## Paranasal sinus endoscope now allows surgery without incision

Sinus surgery that once involved making an incision in the upper lip or in the skin under the eye now may be performed entirely through the nose. The paranasal sinus endoscope, a long, narrow metal probe with lenses and prisms along its length, offers many advantages to physicians, says Dr. Steven Schaefer, associate professor of otorhinolaryngology and one of relatively few physicians in the United States to be doing endoscopic sinus surgery.

"With the endoscope, you can see the disease and tailor the operation to fit the patient. It gives you a lot of versa-

tility," he says. "The big advantage is that you get much less trauma to the patient and potentially more thorough surgery because of improved visualization."

"Visualization" is critical in sinus surgery which is performed in the four small passageways on each side of the face beside the nose and under the eyes. "With the sinus endoscope," says Schaefer, "you can see around corners, which you obviously cannot do with your eyes." Accessories for the endoscope include various probes for angled viewing, an eyepiece, a fiber



Surgeons can "see" the infection with the sinus endoscope.



# Vital Signs

optic cable which helps light the operation and a suction irrigation device for area cleansing during surgery.

Once the endoscope is in the sinus cavity, the physician uses forceps to cut away tissue and bone, opening up the sinuses to let them drain. All is accomplished through the nose.

Chronic sinusitis affects 5 percent of the population. It is caused by allergies, trauma, congenital malformations or diseases involving the cilia in hair cells. Patients may have pain and tender-

ness along the sinuses as well as drainage through the nose and back of the throat. In the serious form of the disease, an obstructed sinus becomes infected, requiring surgery.

Otorhinolaryngologists, allergists and internists will also find the sinus endoscope, when used in conjunction with CT scans, to be beneficial for office diagnoses, says Schaefer.

The German-made sinus endoscope has been used in the United States for only two or three years. ■ *A. McV.*

## Diabetes registry assists research

Parents of a diabetic child live with their fears about the quality of life for their stricken child. They also realize that one or more of their other children could develop the same symptoms at any time.

Diabetes is the most common metabolic disease of Western civilization. Type I diabetes affects at least one or two out of every 100 Americans. This type begins early in life and can cause diabetic coma and death. Fortunately, the discovery of insulin in the 1920s has made death from diabetic coma a rare event. However, diabetes is associated with a devastating array of long-term complications involving the eyes and kidneys as well as nerves and blood vessels supplying the heart and brain. Insulin therapy, which in most cases prevents the diabetic patient from going into coma, does not prevent these complications. Consequently, diabetes is a leading cause in this country of adult blindness, kidney failure and amputations to limbs because of gangrene. Type I diabetes is also a major cause of heart attacks and strokes.

In order to find the answer to the question of who is at risk for juvenile-onset diabetes mellitus, or Type I diabetes, researchers at The University of

Texas Health Science Center at Dallas have launched a major research effort into the genetics of this disease. The first step was the establishment of a diabetes registry of patients with Type I diabetes in the North Texas area. To date 287 families are participating. The first phase of the research program is enlisting the help of 4,000 North Texans with diabetes and their immediate relatives who do not have the disease but who are at increased risk of developing it. Dr. James Marks, associate professor of pediatrics at UTHSCD and director of the diabetes clinic at Children's Medical Center, spent a sabbatical year in Pittsburgh, Pa., in 1984 working with a prototype registry in preparation for starting the Dallas project.

Dr. Daniel Foster and Dr. Roger Unger, both professors of internal medicine at UTHSCD, are directing this project along with other major work that they hope will ultimately lead to cure and prevention of the disease. The two physicians are internationally known researchers in diabetes. Both have received the Banting Medal, the world's highest award for research in diabetes. Unger, especially, has received acclaim for his discovery of the role of glucagon along with insulin in diabetes.

"The diabetes registry is a resource of great value because DNA, the genetic blueprint of the cell, is isolated from the blood cells of each patient and stored for future study," said Foster. As the techniques of molecular biology are increasingly applied to diabetes this DNA will allow detection of the specific genetic defect leading to diabetes in various families. One question that must eventually be answered is whether the genetic susceptibility to diabetes is the same in every patient or whether there are multiple variations. The composite DNA library from the registry may ultimately give some insight into this problem."

The identification of 200 brothers and sisters of diabetics who are willing to participate in long-term studies will allow researchers to look for patterns in the way the disease develops in these volunteers, who are currently free of diabetes.

The development of Type I diabetes requires a genetic susceptibility to the disease, Unger explains. This susceptibility is associated with certain protein markers that can be identified in the laboratory by analyzing blood cells. These markers are designated human leukocyte antigens (HLA) and T-cell receptor antigens.

All participants, including the unaffected brothers and sisters and, whenever possible, parents and children of the volunteer patients with Type I diabetes, are having HLA-tissue typing and tests for the newly discovered T-cell receptor genetic markers. So far there have been 55 sibling "matches."

However, the genetic susceptibility to diabetes alone doesn't cause the disease, pointed out Foster. It is thought that something else triggers the process. That something else seems to be what researchers refer to as an "environmental event," such as a viral infection. ■ *A. H.*