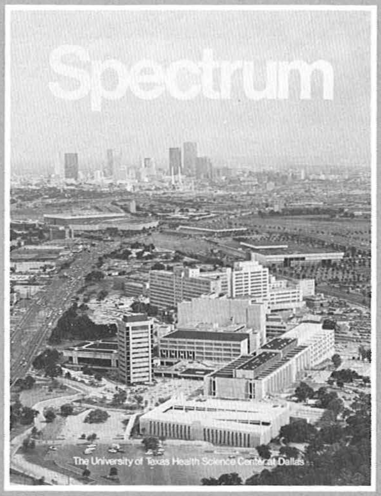
Spectrum

The University of Texas Health Science Center at Dallas

Spectrum

Contents

Spring 1975



ON THE COVER Spectacularly bathed in sunlight, the imposing physical facilities of The University of Texas Health Science Center's expanded campus are seen from the air in this photograph by Bob Cooper of UTHSCD's medical illustration services. Downtown's skyline, also floodlighted by sunshine, is in the background.

A responsibility to the community

As dedication ceremonies officially herald completion of our years-in-the-making expansion program, The University of Texas Health Science Center at Dallas reaches a benchmark in its history. With this remarkable achievement behind us, I can think of no more appropriate time to pause and take a new look at where we are, where we should be and where we should be going in the years ahead.

There is a temptation, with such a major endeavor completed, to be content merely with concentrating on maintaining the quality of education and research for which our institution has become recognized—this is, after all, itself a major task in the face of expanding class sizes and increased teaching programs. But I feel we should not—if, indeed, we could—limit ourselves to "status quo" because we will never stop expanding intellectually and professionally even though a plateau of physical maturity has been reached.

As a state institution, the Health Science Center has an obligation not only to educate students and conduct scholarly research, we have a responsibility to our community. We are, in fact, already meeting this responsibility in numerous ways, some of which go largely unrecognized by major segments of the society which benefits. The value of medical faculty expertise we provide through Parkland Memorial Hospital, for example, is rarely mentioned in discussions of inter-institutional relationships. Other services benefit the community in terms of vastly improved health care, teacher training, clinical applications of research, continuing education of medical practitioners.

It is well nigh impossible to compute the worth to the community of such projects as Children & Youth, which has saved lives and reduced hospital days among West Dallas youngsters; Maternal Health and Family Planning, which provides valuable preventive medical care and birth control services; for medical teaching services donated by Southwestern physicians and surgeons to train Dallas Fire Department ambulance paramedics, giving the city a service matched by only a few in the nation; by providing answers to basic research riddles, such as recently discovered genetic clues of fat metabolism; by giving clinicians new tools, such as the nuclear heart-scanning device which provides a "picture" of a heart attack . . . the list could go on.

But at this stage of our development, we need to look at other possible areas of potential future growth —not at the expense of existing programs but with a goal of selectively choosing those new arenas for service that will further enhance our opportunities for education and research. Here a caution light flashes: certain medical schools and related institutions have moved too far and too fast in the direction of providing services, to the detriment of their basic goals and purposes. A balance must be struck, and admittedly it is a tricky one, between going overboard into community services and failing to move out sufficiently beyond the cloistered walls of academe.

Where, then, do we expand, and by what yardstick? Several factors are involved, and not all of them are within our control: developing community needs, changes in public policy affecting health care delivery, the availability of resources within the public and private sectors, to cite a few.

A basic guideline in selectively meeting new challenges should be that community programs help fill our own needs, such as the crucial requirements for a continuing clientele of teaching patients. New projects may spring naturally from initiatives within our own faculty, staff and students and should be, in effect, field laboratories for meeting our teaching and research goals. Let me repeat: we must be doubly careful not to compromise the quality of existing educational programs, as reflected, for example, in our medical students' consistently high attainment on national board exams.

One emerging opportunity that falls within our guidelines is in helping develop new modes for medical care delivery in small communities and rural areas. A project is being cooperatively initiated betwen the Health Science Center's Department of Community Medicine and a group of physicians in Corsicana, to train more family doctors and support personnel. This will fill a vital and largely unmet need for medical services in many small towns and remote areas, while our students will receive valuable training.

Ideally, our community involvement should be at the threshhold level; that is, our efforts should be experimental, innovative and point in new directions, providing services or facilities at places or in ways not now provided. These programs can serve as models for the future improvement of health services and patient care and should be designed so that at the appropriate time other agencies can take them over. Then we, continuing our climb along a path of leadership, can go on to other things. ■

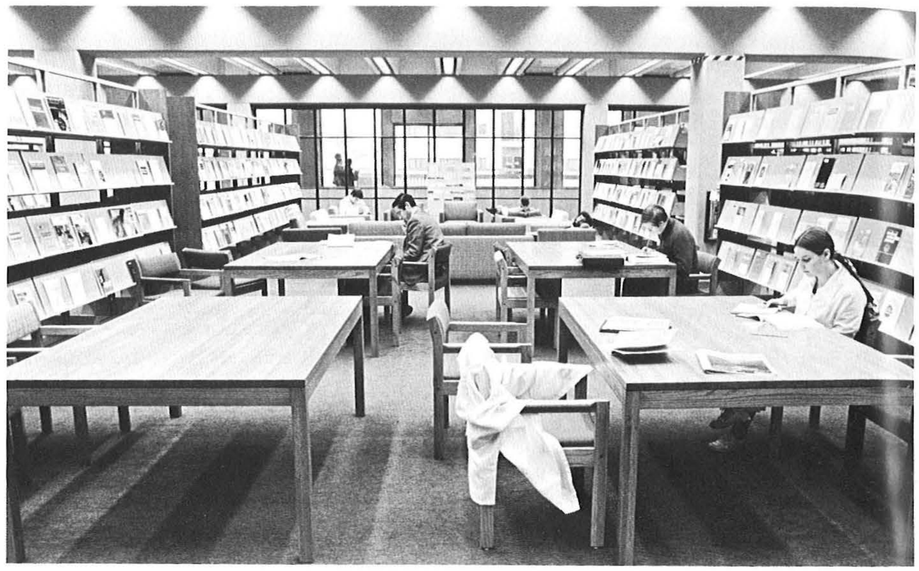
CHARLES C. SPRAGUE, M.D.
PRESIDENT

David Hills

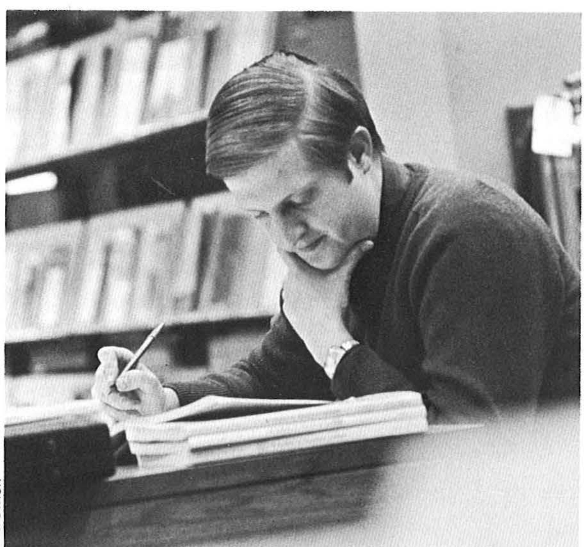
President Sprague (left) escorts Gov. and Mrs. Dolph Briscoe on tour of campus

A Climate for Learning

New facilities afford spectacular setting for activity of students, faculty, staff

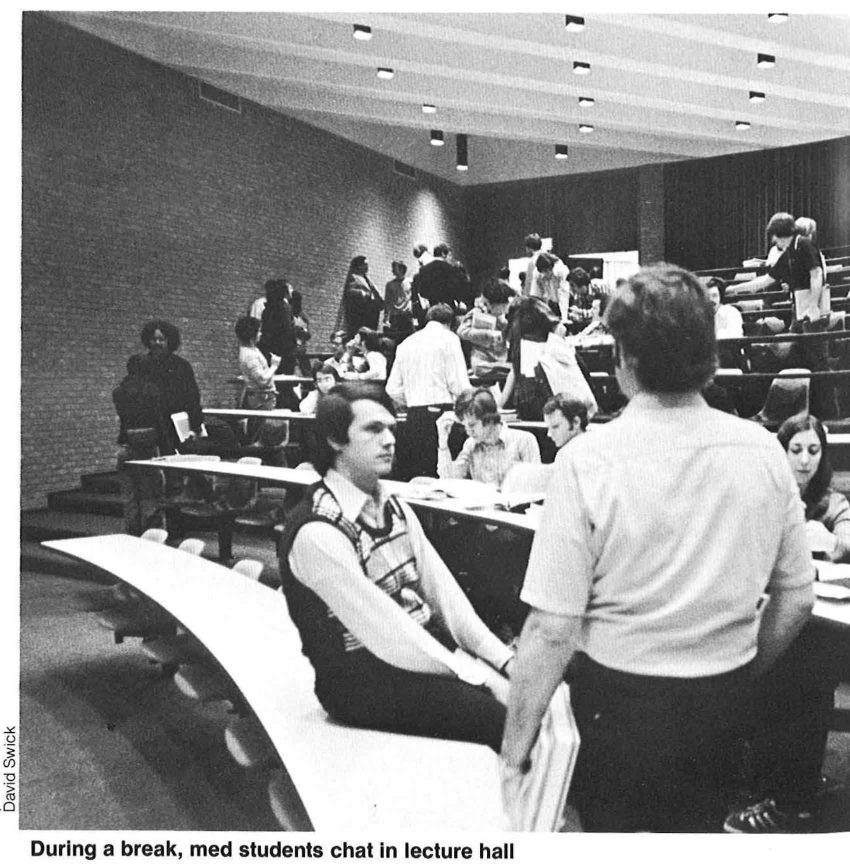


Spacious, well lighted journal section serves more library users



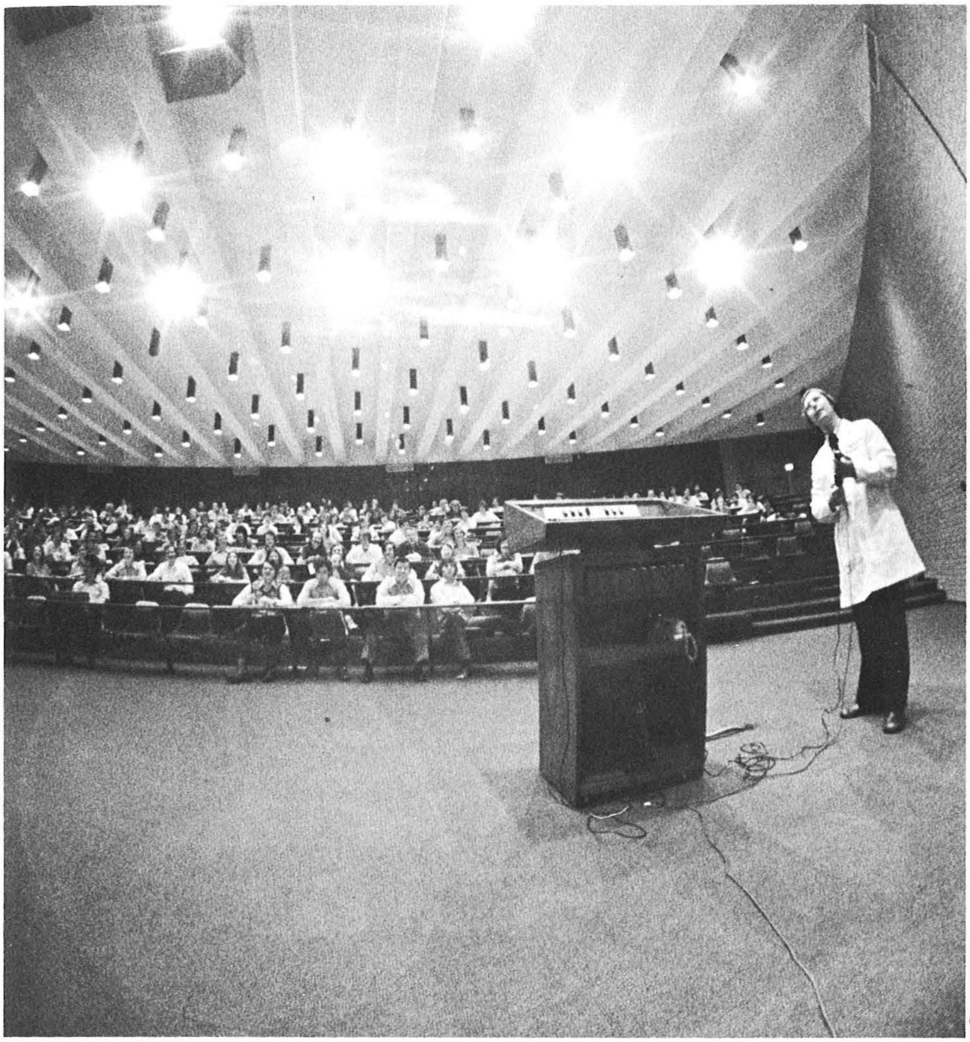
David Swick

In library, concentration is evident



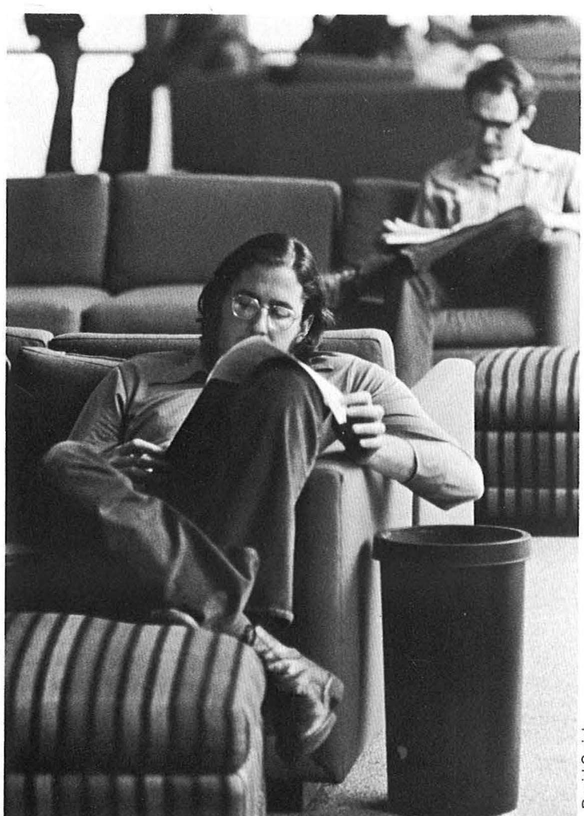
David Swick

During a break, med students chat in lecture hall



David Swick

'Fisheye' camera lens provides spectacular image of new lecture hall



David Swick

Lounge areas afford a comfortable respite

Medical education is a technical or professional discipline; it calls for the possession of certain portions of many sciences arranged and organized with a distinct practical purpose in view.

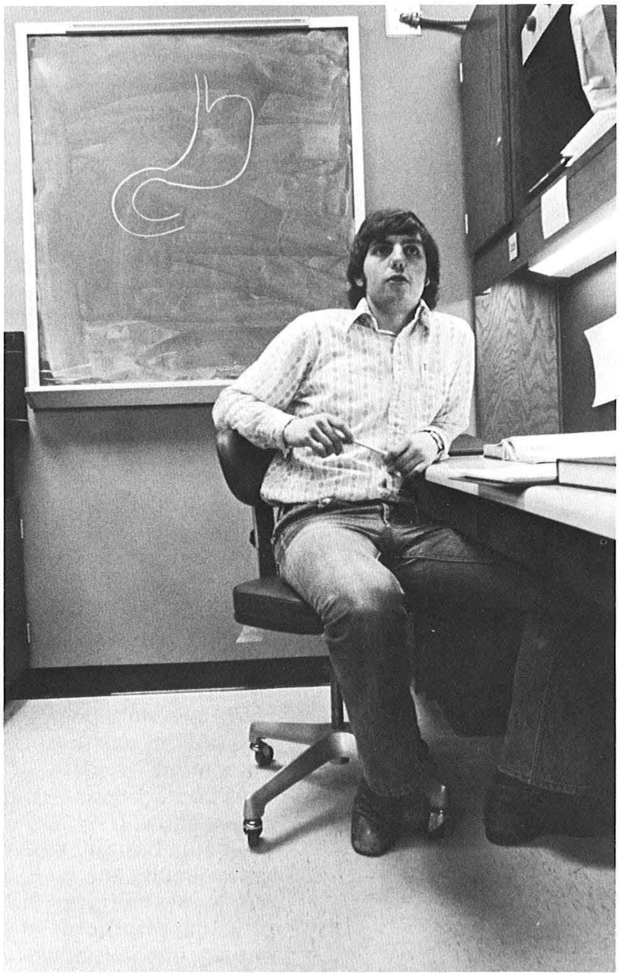
—Abraham Flexner (1866–1959)

The University of Texas Health Science Center at Dallas has realized a long-held major goal—providing an expanded physical facility of the first class in which to bring together medical teachers, scientists and related personnel to provide expanded education and research for a broad spectrum of health care needs.

Last fall, the magnificent new Phase One building program was completed and put into use—a functional, beautiful arena for studying, teaching, working in varied ways toward useful objectives. This spring, official dedication ceremonies hosted by The University of Texas System Board of Regents were to officially celebrate completion of some $50 million worth of new plant and equipment.

As photographs on these and following pages show, UTHSCD's building program has brought students, as well as many faculty and staff, a new environment—and has given the institution a new physical character of spectacular impact. Images shown here are intended to depict that new environment as seen by its users. Some highlights:

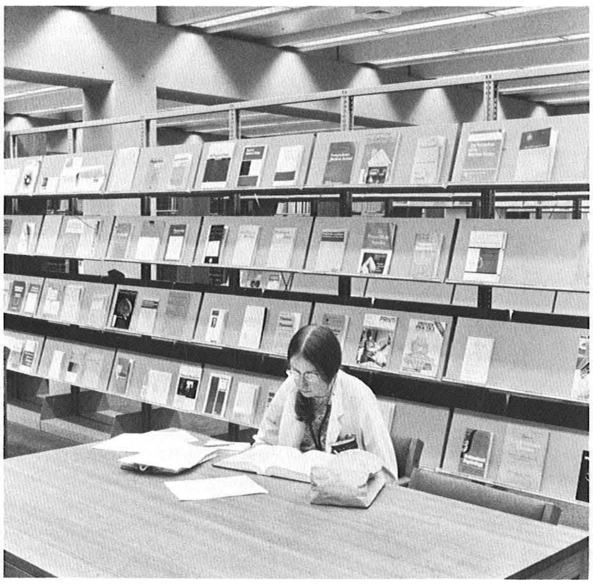
- Four new lecture halls accommodating medical school classes expanded to 200 each, nearly twice the size of a few years ago;
- An excellent and vastly expanded library, with latest in information retrieval systems;
- Modern audiovisual facilities for enriching techniques for teaching;
- New research laboratories which expand the center's capacity for scientific inquiry;
- Individual laboratories to give first and second-year medical students their own special work and study area;
- The first auditorium and cafeteria facilities in the institution's history;
- New lounges to enhance students' leisure time ; and seminar rooms for a variety of academic pursuits.
- An imposing 12-story office tower giving the campus a "skyline"; and a handsomely landscaped plaza—providing a new visual and geographic focus.



David Swick

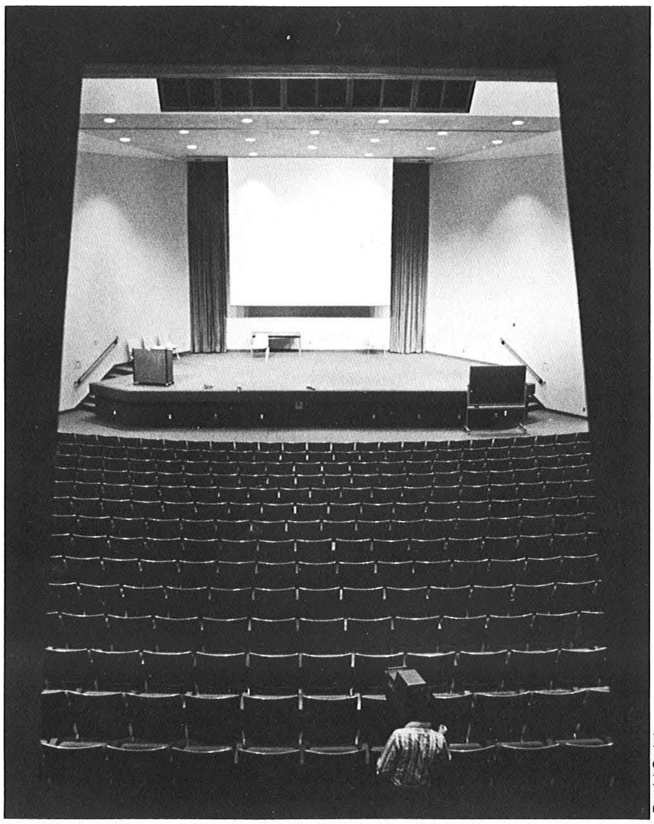
Individual labs provide med students' own study niche

Models for use in learning about the eye 'stare' from library study carrels



Dan Barsotti

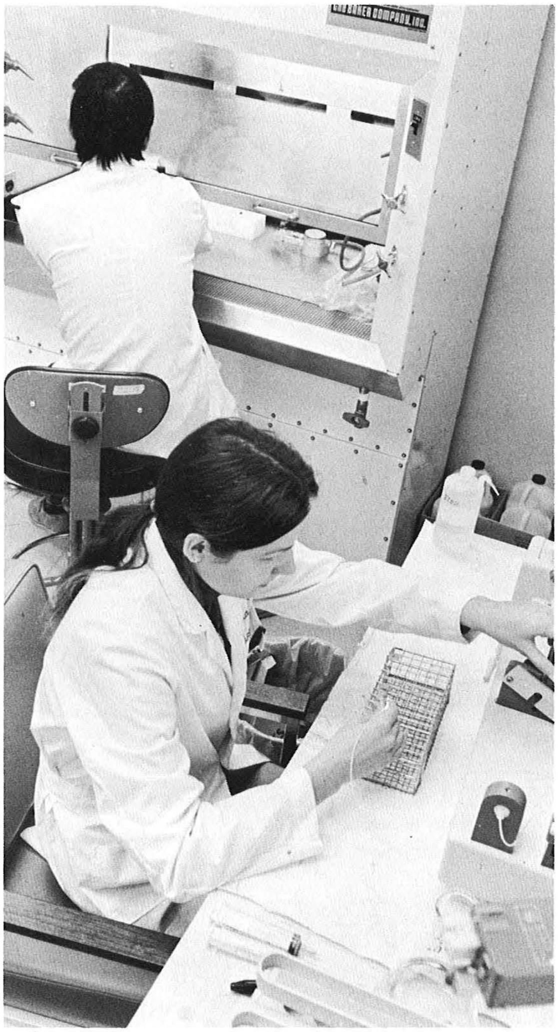
It's study time—with lunch not far away



David Swick

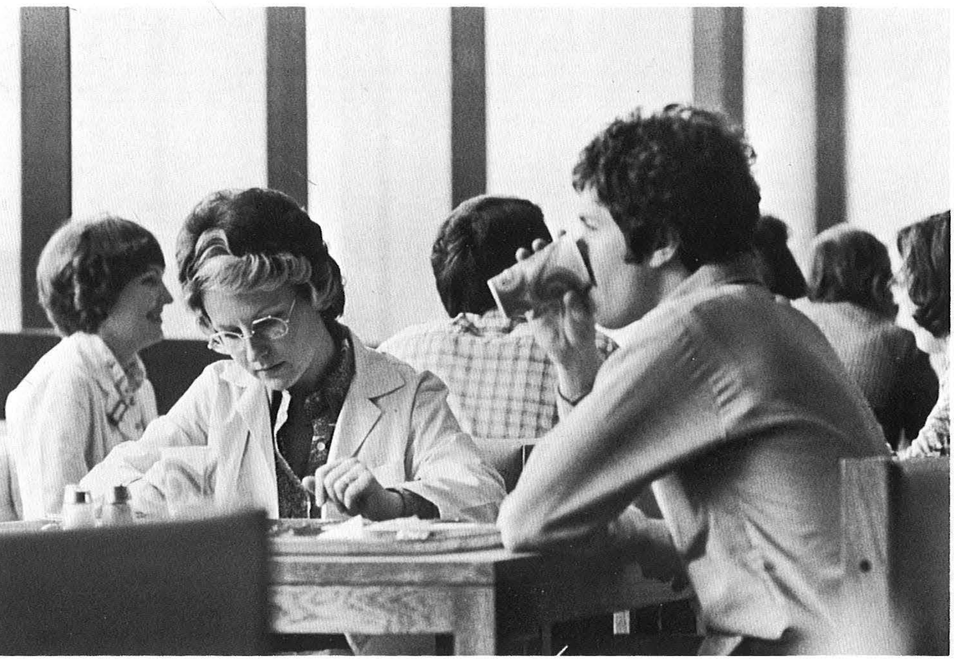
Projectionist's-eye view of new Gooch auditorium

Dan Barsotti



David Hills

Technicians use latest equipment in new research laboratory



Campus' first cafeteria enjoyed by students, staff

David Swick

The additions raise the Health Science Center's size from half a million square feet of space to 1.2 million.

Culmination of the Phase One building effort marked the realization of a concept to expand The University of Texas Southwestern Medical School into a multidisciplinary health science center with increased enrollment capacity of medical, science and allied health students.

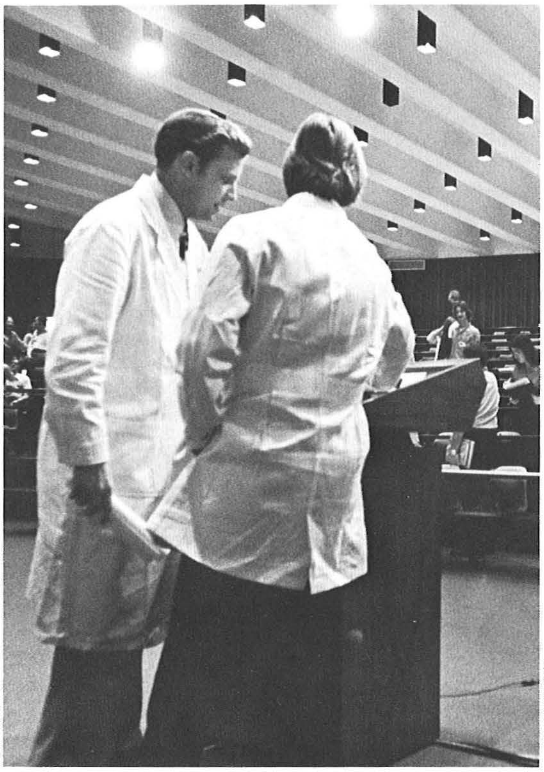
This initial concept was put in motion by Dr. Charles C. Sprague shortly after he became dean of Southwestern in 1967. Responding to a public need for additional doctors and other professionals, a task force led by Dr. P. O'B. Montgomery drafted the Phase One plans, aided by a number of faculty committees.

Southwestern was reorganized and renamed The University of Texas Health Science Center at Dallas, in action by the UT Board of Regents in 1972, with three component schools—Southwestern Medical School, the Graduate School of Biomedical Sciences and the School of Allied Health Sciences.

Funding for the expanded Health Science Center was provided by the National Institutes of Health, Southwestern Medical Foundation and The University of Texas System. Construction on Phase One began May 10, 1971.

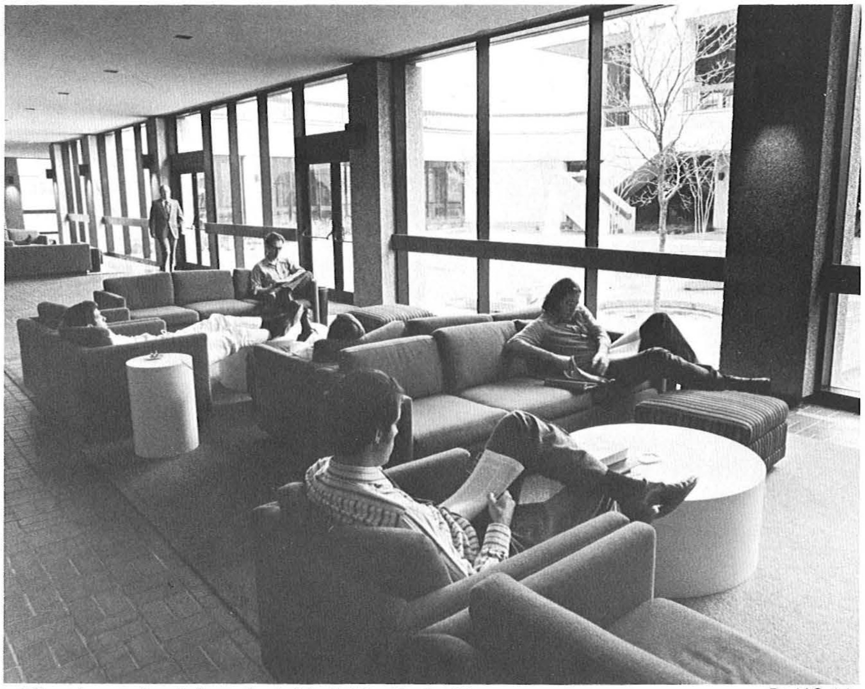
An additional expansion of center facilities is already under way, with construction in progress on the Harry S. Moss Clinical Sciences Building, named in honor of the late oilman whose will provided a generous bequest for use in pursuit of the cure and prevention of heart disease. Completion of this structure is scheduled in 1977.

In addition to the Moss building, the April ceremonies officially dedicated these new campus landmarks which

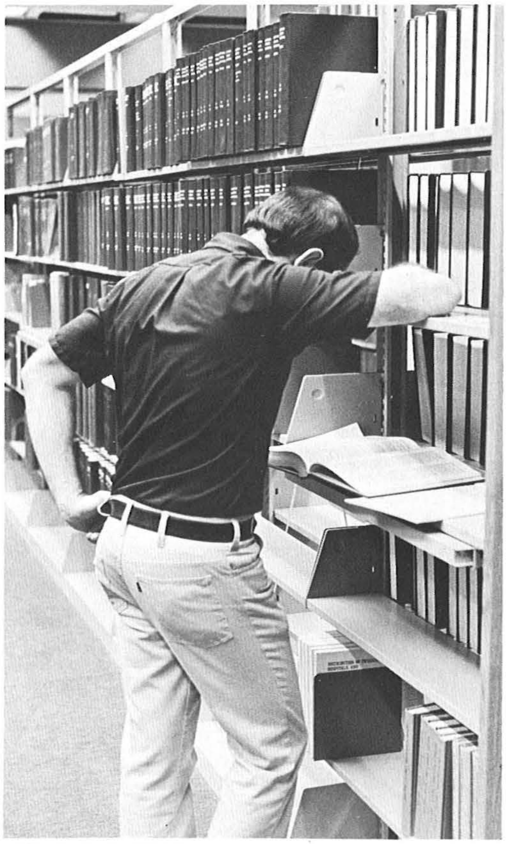

David Swick

Faculty conference precedes start of lecture


Ample facilities, pleasant atmosphere keynote new cafeteria

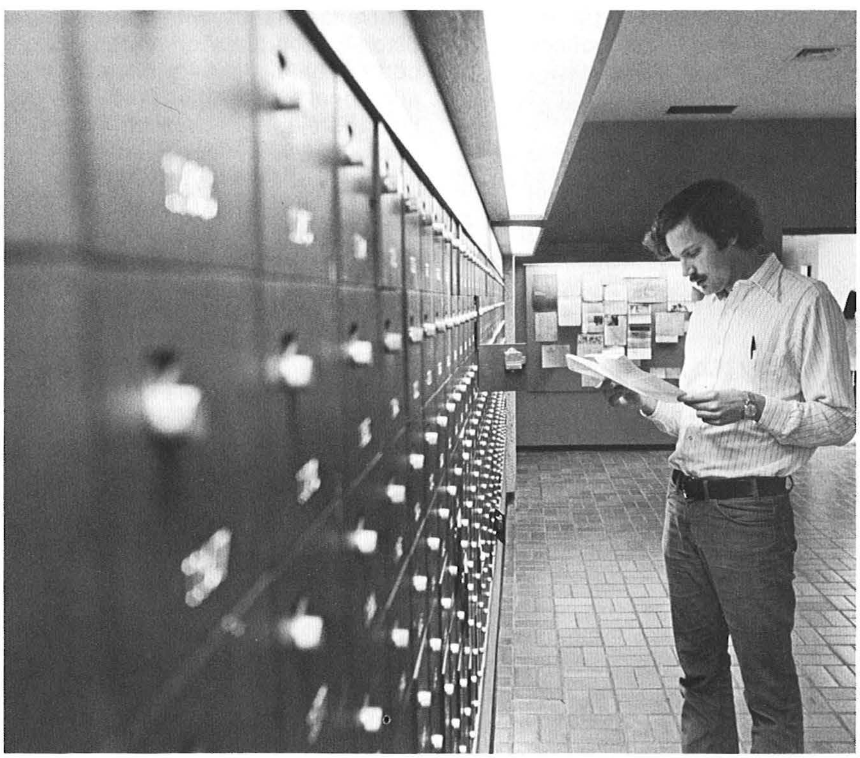

Plaza's garden brings 'outside in' to student lounge area

David Swick


David Swick

Bookcase affords spot for impromptu study

Three levels of new library
are visible in this dramatic perspective



First lockable mailboxes are a feature of new student facilities

made up the Phase One project:

• The Eugene McDermott Academic Administration Building, a 12-story, 57,526-square-foot office tower surmounting the entire Phase One complex.

• The Tom and Lula Gooch Auditorium, a 1,200-seat facility of 29,966 square feet, with a cafeteria of similar size on the lower level seating 500 plus four small dining rooms.

• The Fred F. Florence Bioinformation Center, a five-story building housing a medical library of 200,000 volume capacity, plus Southwestern's historical book collection, faculty center, and facilities for Instructional Communications, Medical Computing Resources Center, Medical Illustration Services and other offices.

• The Cecil H. and Ida Green Science Building, a five-story structure containing the most up-to-date research laboratory and departmental facilities plus multipurpose student labs and seminar rooms.

• An elevated plaza connecting all the new buildings, under which are located, in a pie-shaped configuration, four large lecture halls with a central audiovisual core, plus lounge and snack areas. Total area of the Green building and plaza is 346,200 square feet.

Dr. Lewis Thomas, accomplished medical scientist and writer who is president of Memorial Sloan-Kettering Cancer Center, was to be speaker for the dedication event, which was to be presided over by former Gov. Allan Shivers, chairman of the UT System Board of Regents. Several hundred persons were invited guests at the dedication, and the facilities were to be toured by hundreds more during a public open house that concluded the April 27 event. ■

DIABETES: double trouble

UTHSCD scientist's trailblazing research shows obscure hormone—glucagon—causes 'other half' of blood-sugar disease process

By JOHN WEEKS

During the half-century since the discovery and utilization of insulin, medical science actually has been treating only half the disease process involved in diabetes, an award-winning UTHSCD scientist believes.

Dr. Roger H. Unger says recent research findings strongly support the thesis that blood-sugar balance is maintained by not just one but two hormones working in counterbalance, with a lesser known substance also secreted by the pancreas—glucagon—playing an essential role along with insulin lack in the metabolic disorder in which normal blood-sugar balance goes haywire.

These developments suggest the possibility of improved treatment and better control of the disease in the future, says Dr. Unger, professor of internal medicine at UT Southwestern and chief of medical research at Dallas' Veterans Administration Hospital.

For his pioneering work in steering diabetes research into a promising new direction, Dr. Unger recently was named recipient of the Banting Medal for 1975, highest scientific honor bestowed by the American Diabetes Association. He will receive the medal and deliver the Banting Memorial Lecture during the association's annual meeting June 14–17 in New York.

In announcing Dr. Unger's selection, ADA President Dr. Max Ellenberg said the Dallas scientist's "pioneer work with glucagon . . . has established him at the very forefront of all diabetic investigation at this time."

The Banting Medal is regarded as one of the most prestigious honors among researchers in metabolic disease. It is named for the late Sir Frederick Banting of Toronto, co-discoverer with Dr. Charles H. Best of the function of insulin in 1922. Their work paved the way for the first successful treatment of diabetes. Dr. Best is among prominent past recipients of the medal, first awarded in 1941.

Numerous other awards have come Dr. Unger's way, including the Veterans Administration's Middleton Award, the Lilly Award of the American Diabetes Association and two citations from the ADA's Texas affiliate for "most significant work in his field." He will also receive the 1975 Research Award of the National Juvenile Diabetes Foundation later this year.

Two decades of painstaking investigation by Dr. Unger has played a major role in the recent broadened concept of diabetes—that it results not only because insulin is insufficient (the defect Drs. Banting and Best corrected) but because glucagon is present in excessive amounts, stimulating the liver to produce even more glucose, or blood sugar, and thus compounding the problem.

"When a normal person eats carbohydrates, glucagon turns off instantly," Dr. Unger explains. "But not in diabetics. Continued secretion of glucagon—a hormone that raises the blood sugar level—means that insulin has to fight a hormone that opposes it." Consequently, with current therapy, diabetics require even more insulin to control the disease—because of the additional blood sugar produced by glucagon—than is present in normal persons.

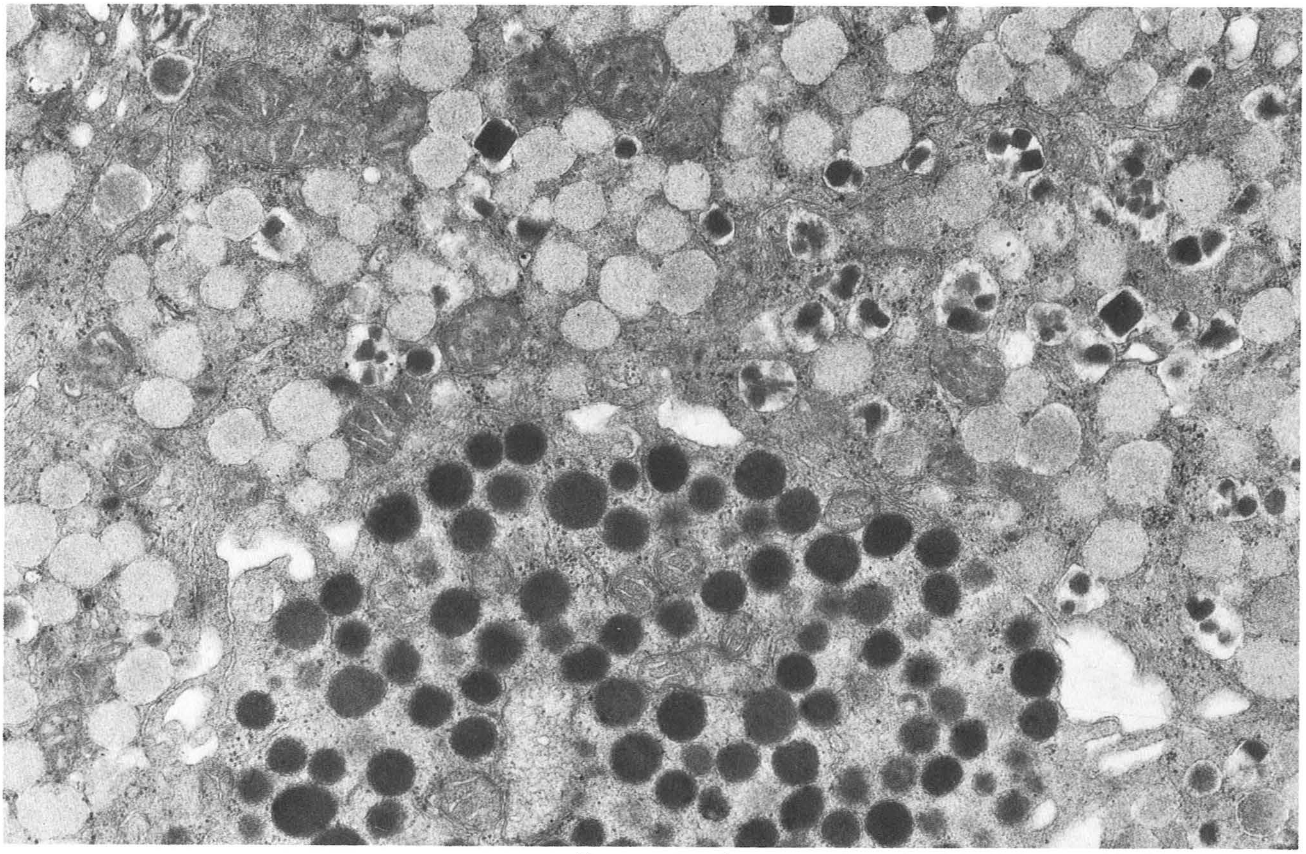
In recent weeks, two major scientific publications have published reports by Dr. Unger and his associates detailing important new findings implicating glucagon in the diabetic process.

In the British medical journal Lancet, Dr. Unger and Dr. Lelio Orci of the Institute of Histology and Embryology in Geneva outlined the "bi-hormonal abnormality hypothesis," which in essence says that diabetes is twice as complicated a disease as has been recognized, and existing insulin therapy deals with only half the problem.

Dr. Orci, who holds an adjunct professorship at Southwestern, and Dr. Unger worked together in Geneva during 1972–73.

Writing in the Feb. 14 issue of Science magazine, Drs. Unger, Orci and others including Dr. Richard Dobbs of the Southwestern physiology faculty detail animal experiments which "suggest that the development of diabetic hyperglycemia (high blood-sugar) does, indeed, require the presence of glucagon."

When both insulin and glucagon are suppressed to "unmeasurable concentrations" by a new experimental hormone called somatostatin, the excessive blood-sugar disappears—unless glucagon concentrations are



Two pancreas hormones show clearly in highly magnified view from lab of Dr. Lelio Orci: round clusters below are glucagon molecules; squarish shapes above are insulin

restored.

This suggests, they report, "a potentially valuable new approach to the treatment of diabetes."

Somatostatin, still in experimental development, has been used by West Coast scientists in tests of human diabetics with similar results, they note. Somatostatin was discovered last year by Dr. Roger Guillemin at California's Salk Institute.

"Suppression of glucagon (in experimental animals having artificially induced diabetes) results in rapid reduction of hyperglycemia" to below-normal concentrations, the Dallas scientists wrote.

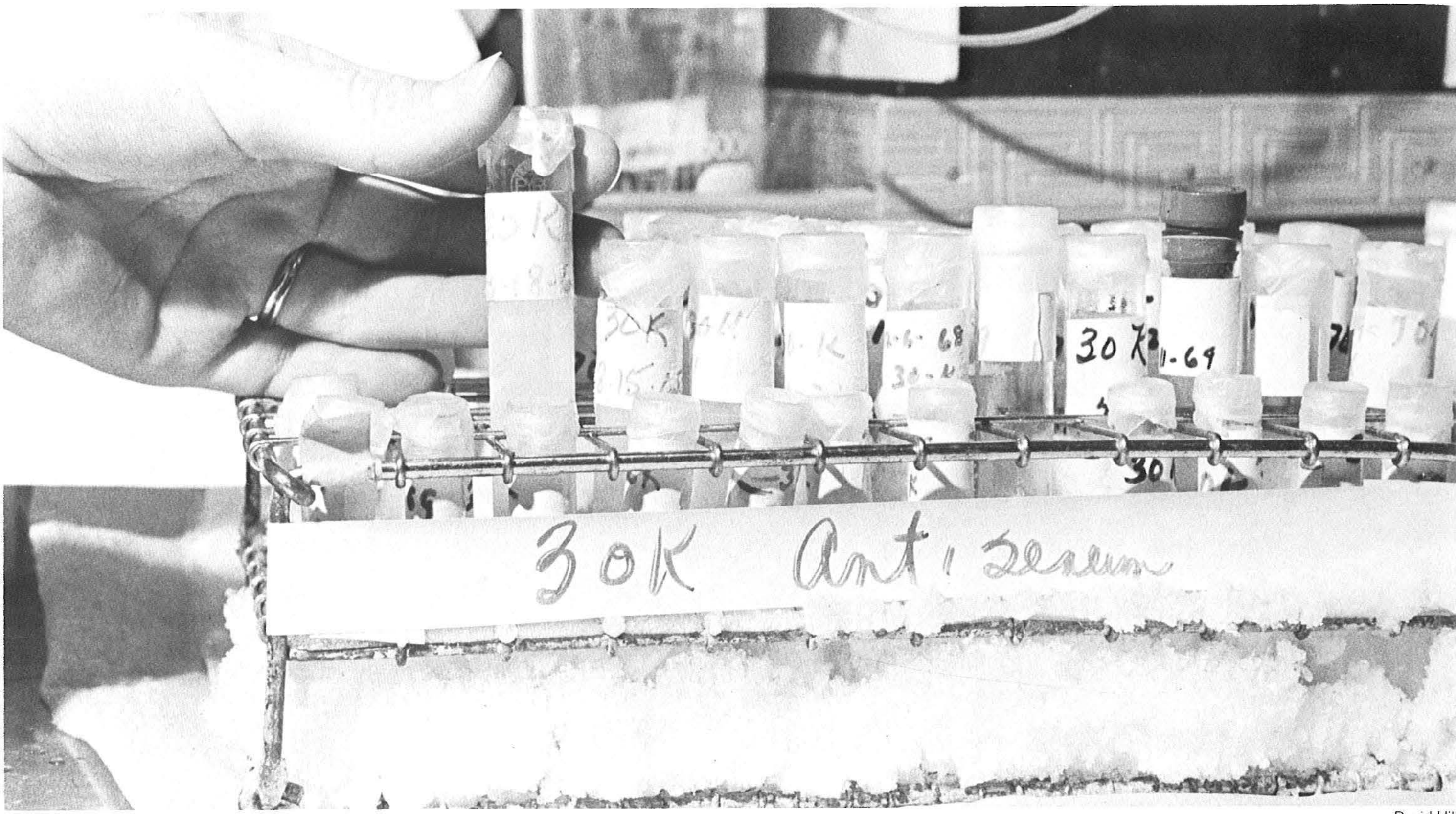
Dr. Unger's trailblazing work has laid the basis for wide experimentation into the "other side" of the diabetic syndrome. A key factor in much of the increasing research interest was the development in his Dallas VA hospital laboratories of a complex technique for measuring minute quantities of glucagon in the blood. The radioimmunoassay process, utilizing radioactive iodine to "tag" glucagon molecules, has enabled others to join in the study of glucagon.

Helped greatly by a cooperative rabbit which developed large numbers of glucagon antibodies, the Dallas lab has supplied the rabbit's serum containing these antibodies to dozens of laboratories in many nations.

Although rabbit "30K" has now died, enough of his serum is retained in freezers to supply researchers at the

David Hills

Dr. Roger Unger (right) studies micrograph enlargements of pancreas cells with associate Dr. Richard Dobbs



David Hills

Blood samples from the late Rabbit '30K' still provide means of glucagon testing

David Hills

Technician Cathy Mitchell works in Dr. Unger's VA lab

present rate for several more years, Dr. Unger says. Each small vial is sufficient for 1,000 diagnostic tests. In tribute to the animal's contribution, Dr. Unger's assistants have had Rabbit "30K" stuffed and he continues to occupy a special niche in the lab where he made his contribution to science.

Finding a means of glucagon suppression is now a major goal of many diabetes researchers, including Dr. Unger. But, he says, glucagon has become an area of major scientific interest in only the last four years. And hard evidence as to its function was unearthed only recently.

"Until last year, nobody could say it would have been possible to suppress glucagon," the Dallas scientist notes. "Secondly, nobody could say that if you could suppress glucagon, that it would ameliorate diabetes.

"But now both those questions have been answered. We can suppress glucagon and it does permit a remarkable amelioration. Blood sugar drops dramatically."

Up until only a few months ago, he explained, there was no alternative but to attribute diabetes totally to a lack of insulin. That was before experiments dramatically demonstrated that all glucagon was not coming from pancreatic cells.

Researchers removed the pancreas in animals and glucagon levels remained high—an "impossibility" according to prevailing scientific thought, because the pancreas contained all cells then

Margaret Bickham prepares samples for glucagon experiment

Giant beaker holds solution for Dr. Coimbatore Srikant

known to produce both insulin and glucagon.

This sent Dr. Unger and other scientists back to the drawing board. Further search turned up "alpha" cells identical in structure to those which secrete glucagon ("beta" cells turn out insulin) in the pancreas.

"There are alpha cells in the top of the stomach and the upper small intestine," Dr. Unger says. These new-found cells are believed to provide a backup mechanism for producing glucagon. And their discovery helped prove convincingly that glucagon's presence is required for diabetes to occur—turning upside down the conceptual picture of diabetes, which heretofore had focused solely on the pancreas.

"The minute we found that you are removing only half the glucagon-producing tissue when you remove the pancreas, then it became possible to entertain the notion that glucagon was essential to diabetes," Dr. Unger said.

Dr. Unger's group has found excessive glucagon levels in more than a dozen forms of diabetes—further evidence, he says, that the overlooked hormone is necessary to the disease process.

The effect of recent studies, Dr. Unger said, is to show that two things actually are happening in glucose metabolism:

"First, there is a reduced ability to use sugar that comes in your diet, and that's due to insulin lack. That can be corrected only by giving insulin or something similar.

"The second abnormality is that even if you are not eating, your liver overproduces glucose at a rate which exceeds the needs of the body, so that the blood sugar rises. That is due to glucagon. And that should be corrected by suppressing glucagon."

The scientific premise of a two-component disorder—one due to insulin lack, the other to glucagon excess—"wasn't appreciated until now," he noted.

What does all this mean to the diabetic patient?

"Recognition of this premise opens a whole new avenue for investigation of the control of diabetes by an entirely new approach," Dr. Unger said. "I think it really does raise tremendous hope for a new form of therapy—the development of a chemical agent, either a form of somatostatin or some other substance, which will suppress or block glucagon, so that the balance of the effects of insulin and glucagon are closer to normal."

Now, in Dr. Unger's opinion, there is no such thing as an optimally controlled diabetic.

"Blood sugar normally stays within a narrow range in response to how much you eat or exercise," he said. "But the diabetic doesn't enjoy that luxury. When he eats, blood sugar goes 'way up. When he exercises, it goes 'way down. It can't be kept in a normal range.

"We hope this new approach will make that possible."

When might large-scale suppression of glucagon in diabetics be achieved? This depends, Dr. Unger asserts, on how actively the pharmaceutical industry and medical science generally takes up the search for an appropriate agent. (Somatostatin, encouraging as it is, lasts only a short time and is thus far not ready for widespread use.)

He stresses that only after long years of further study, once glucagon is controlled and a better blood-sugar balance achieved in the diabetic patient, can it be determined whether the physiological problems believed associated with the disease, such as blood vessel, eye and kidney changes, will be helped by improved diabetes treatment.

But clearly he is optimistic. And if there remains a long way to go, it's also true that he and his colleagues have traveled a considerable distance already. Glucagon was not even thought to be a hormone when he began his Dallas studies after joining Southwestern's faculty in 1956.

"Now," he notes with pride, "it is recognized that excessive glucagon secretion is one of the most common of all endocrine disorders."■

Key Clue to Cholesterol Mystery

By BOB FENLEY

UTHSCD team discovers the genetic factor responsible for one type of blood-fat disease —and reaps unexpected scientific harvest

It took a while. First of all, wiring in the Clinical Sciences Building wasn't adequate for the incubators and there was a problem with carbon dioxide deliveries. Not to mention infection. But in December, 1972, some four or five months after they started, researchers Joseph Goldstein and Michael Brown succeeded in getting test tube cultures of skin cells to perform some interesting acts of fat regulation.

From that point the two scientists at The University of Texas Health Science Center at Dallas were able to move to prove that a specific genetic factor is responsible for a kind of high blood fat disorder which afflicts one out of every 500 Americans.

What doctors Brown and Goldstein didn't realize at the beginning was that the work would open up an entirely new avenue of research:

"We've gotten an unexpected dividend," says Dr. Goldstein. "It's the first good handle on the biochemical mechanism by which cholesterol is laid down."

Cholesterol is the chief ingredient of the fatty plaques which coat the insides of arteries and eventually cause coronary heart attacks and other ills of blood circulation. Cardiovascular

Dan Barsotti

Human cells, grown in laboratory, are 'harvested' for use in cholesterol studies

Dan Barsotti

Technician Mary Sobhani takes sample for cell test

disease today is the chief killer of Americans.

The new find which excites the researchers involves cell lines derived from a 12-year-old girl with the genetic defect which causes high blood fat—familial hypercholesterolemia— and from normal youths. The scientists were able to manipulate cells so as to reveal the existence of a hitherto unknown protein linked in a chain of biochemical events inside the cell. This procedure provides an excellent test bed for ferreting out the formation and regulation of cholesterol.

The work really got started back in 1966 at Massachusetts General Hospital where Goldstein and Brown became acquainted during their internships and residencies. Dr. Goldstein was a product of The University of Texas Southwestern Medical School where he took the school's top honor —the Ho Din Award. Dr. Brown was from the University of Pennsylvania School of Medicine where he won the Frederick L. Packard Prize in Internal Medicine in the same year.

The two young doctors had similar interests in genetic and metabolic diseases and, on seeing patients whose high blood fat seemed to have family ties, started cranking out preliminary concepts.

In 1968 Dr. Brown joined the National Institutes of Health as clinical associate in the Digestive and Hereditary Disease Branch. In the same year Dr. Goldstein joined the NIH as clinical associate in the Laboratory of Biochemical Genetics of the National Heart Institute.

Dr. Goldstein really began moving on the familial hypercholesterolemia (FH) problem, however, in 1970 when he went to the University of Washington School of Medicine as a special NIH fellow in the Division of Medical Genetics.

Over most of a year in 1970, Dr. Goldstein studied heart attack victims in Seattle. There were 1,166 admitted to 10 Seattle hospitals and, of these, 885 survived three months or more. The group led by Dr. Goldstein really homed in on 500 of the survivors and 2,520 of their families.

The group found that 31 per cent of the survivors had either high cholesterol or triglyceride levels (or both). Actually, four per cent had FH, five per cent inherited high triglycerides and 11 per cent had inherited both. Of the other 11 per cent, causes were non genetic.

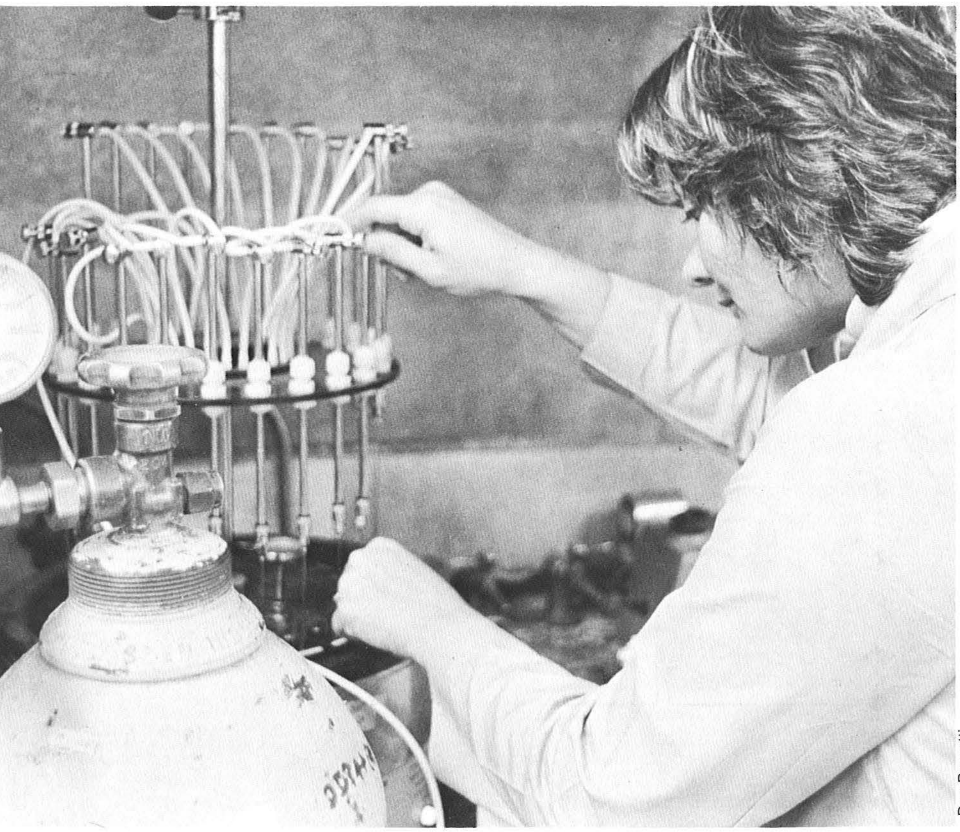
The researchers calculated that one out of every 150 Americans carries genes which cause either high cholesterol, high triglycerides or a combination of the two (which happens to be a separate, specific defect).

Only one out of every five people with high blood fat seems to have inherited the disorder but the people with the genetic form apparently are at greater risk from heart attacks.

There are very rare cases—one in a million—where the child gets the faulty genes from both parents. While blood fat levels for those who get faulty genes from only one side — the "heterozygotes,"—have cholesterol levels two to three times normal and expectation of heart attacks between 40 and 60, the unfortunate "homozygotes" who are doubly cursed with genes from both parents have cholesterol levels four to eight times above normal. They have fatty tumors called xanthomas over their skins and almost all die of heart attacks before 30.

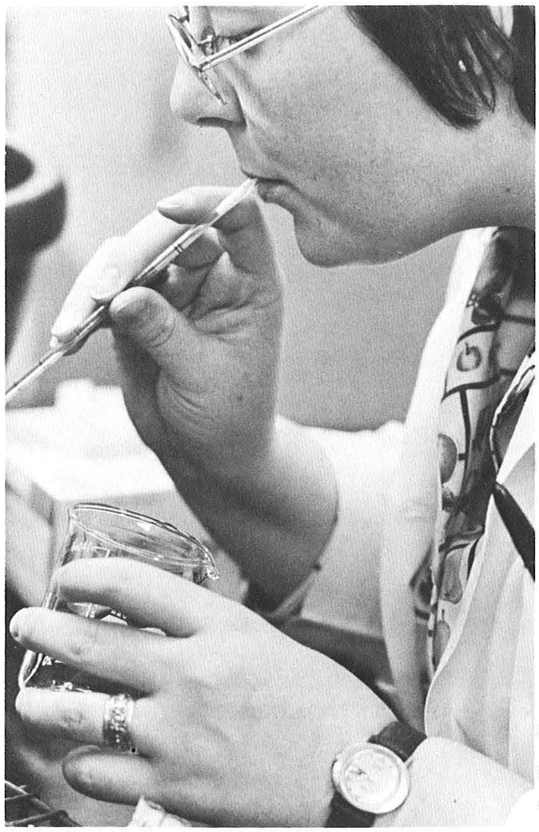
What was happening? How did the genetic information get translated into a fatal metabolic problem?

In 1971, Dr. Brown came to Southwestern Medical School as a research fellow in gastroenterology in the Department of Internal Medicine. A year later Dr. Goldstein returned as head of the Division of Medical Genetics in the internal medicine department.



Dan Barsotti

Using evaporator, Gloria Brunschede 'dries' cell mixture before measuring enzyme activity



Dan Barsotti

Solution transferred by Jean Helgeson

Conventional wisdom had it that what was causing the excess cholesterol was a process involving only the liver cells and that to study the problem one would need to study the whole liver in the whole man—a problem extremely hard to get at in a proper manner.

So Brown and Goldstein decided to flaunt conventional wisdom.

"It's simply the fact that we applied and put together two technologies—cell culture and lipid metabolism," says Dr. Brown. "People hadn't considered you could study the problem in cultured cells."

When Drs. Goldstein and Brown got the broths of skin tissue going—in effect, creating a culture laboratory and methodology where there had been none before—part of the puzzle began unraveling.

What was happening was beginning at the surface of the cell.

In normal persons, each cell has about 250,000 chemical receptors which bind or hook onto low density lipoproteins which are a major chemical form of cholesterol in the blood.

When this normal bond is formed, there are two results: First, a message is somehow sent inside the cell that turns off or, at least, turns down the production of an enzyme which helps produce cholesterol in the cell and, secondly, the low density lipoprotein itself is degraded. Both functions hold down the amount of cholesterol.

When the researchers looked at the cells of those who inherited FH from one or both parents, they began to see differences from the normal.

The heterozygotes with the gene from one parent showed to have only about half the number of normal cell receptors to bind low density lipoprotein.

The homozygotes with the gene from both parents showed practically no receptors at all. This means the production of the key enzyme, called 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase), was not suppressed by any receptor-lipoprotein binding. The result was that HMG-CoA reductase continued playing the role of catalyst for biochemical reactions resulting in the production of large amounts of cholesterol.

Even when the workers added large amounts of low density lipoproteins to the cultured cells of the homozygotes, they continued to synthesize cholesterol at a rate 40 to 80 times higher than normal cells.

The next obvious question was: "Is there any chemical—perhaps closely resembling cholesterol—which could 'fool' the cells into suppressing HMG-CoA reductase and thereby turn down cholesterol synthesis?"

The researchers tried 47 steroid compounds and found that 11 of them actually were more potent than cholesterol and one, 7-Ketocholesterol, was 100 times as strong. They seemed to bypass the receptor mechanism.

While the synthesis of too much cholesterol in the cell leads to the unfortunate result of hyperlipidemia and heart disease, too little availability of the chemical has its own problems.

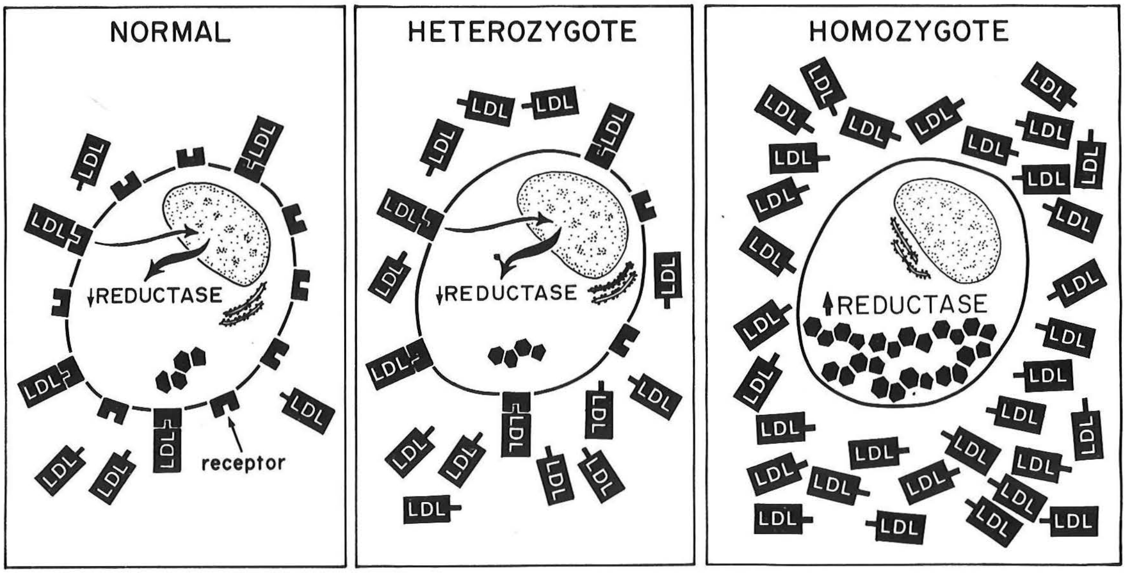
When Drs. Brown and Goldstein cultured normal cells in a medium containing 7-Ketocholesterol but without lipoproteins, growth of the cells was markedly inhibited.

So HMG-CoA reductase looked more and more important as both a rate-controlling factor for cholesterol synthesis and for cell growth itself.

"It is concluded that 7-Ketocholesterol may provide a powerful tool for delineation of the mechanism by which cholesterol and other steroids promote the growth of human cells in culture," the two scientists wrote in "The Journal of Biological Chemistry."

"This gets us into a whole new area. It has tremendous implications for studying the growth of cells,"

FAMILIAL HYPERCHOLESTEROLEMIA
Model for Pathogensis



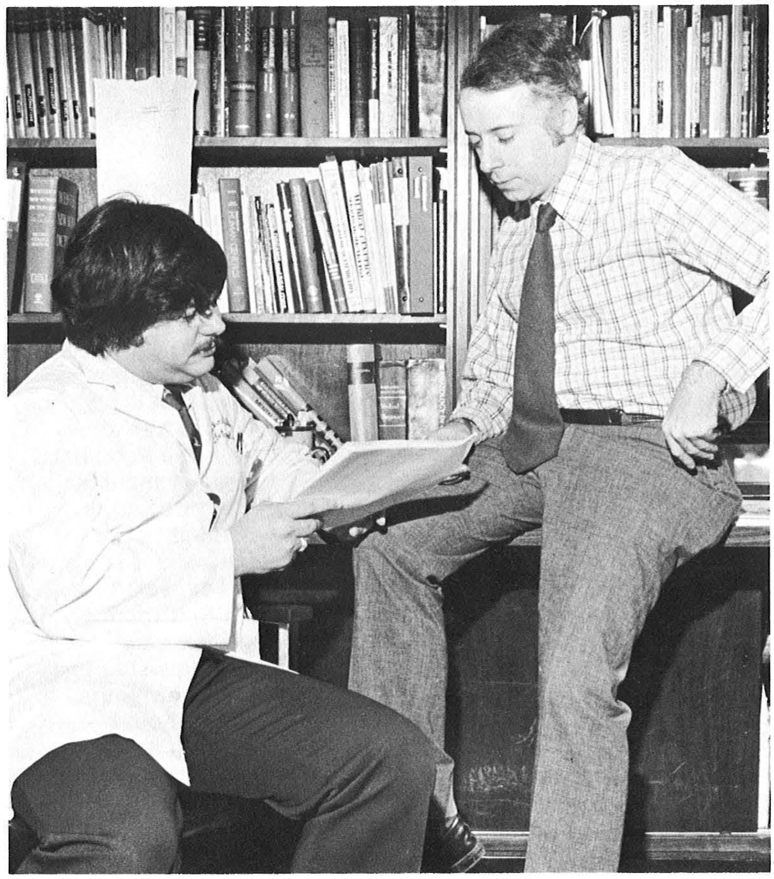
says Dr. Goldstein.

The importance of such knowledge could hardly be overstated. Dr. Brown cites research showing cholesterol may begin to accumulate in early childhood. In fact, the smooth muscle cells inside the arteries can accumulate cholesterol even though blood cholesterol levels are normal.

The current scientific work has been recognized through support by grants from the American Heart Association and National Institutes of Health. Drs. Goldstein and Brown were awarded the Heinrich Wieland Prize last fall in Munich, Germany. Named for a 1957 Nobel Prize winner, the award is one of Germany's most prestigious scientific citations.

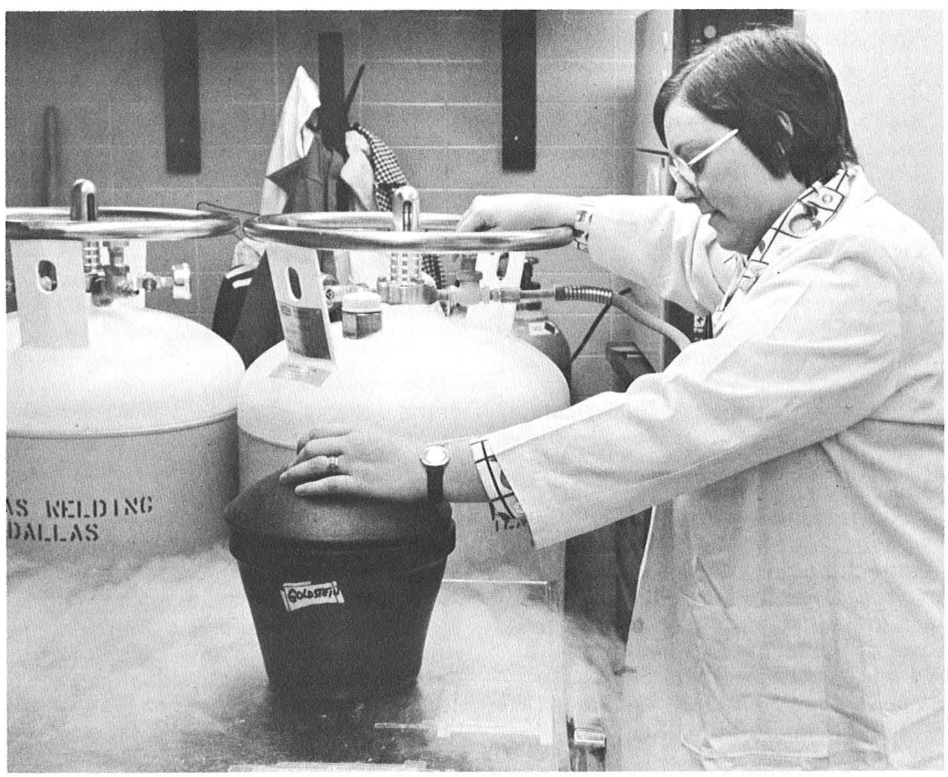
The two researchers paid tribute to their associates and lab workers. They include Helen Bohmfalk, Gloria Brunschede, Suzanna Dana, Jerry Faust, Jean Helgeson, Mary Jo Harrod, Sue Joiner, Dorothy Lund, Denise Richardson, Marva Shaw and Mary Sobhani.

The search, which has many aspects of an elaborate mystery novel, continues at Southwestern with the scientists knowing full well it may never yield another answer or that it may solve the mystery of coronary heart attacks tomorrow. ■



David Hills

Drs. Michael Brown (left), and Joseph Goldstein discuss experiments



Dan Barsotti

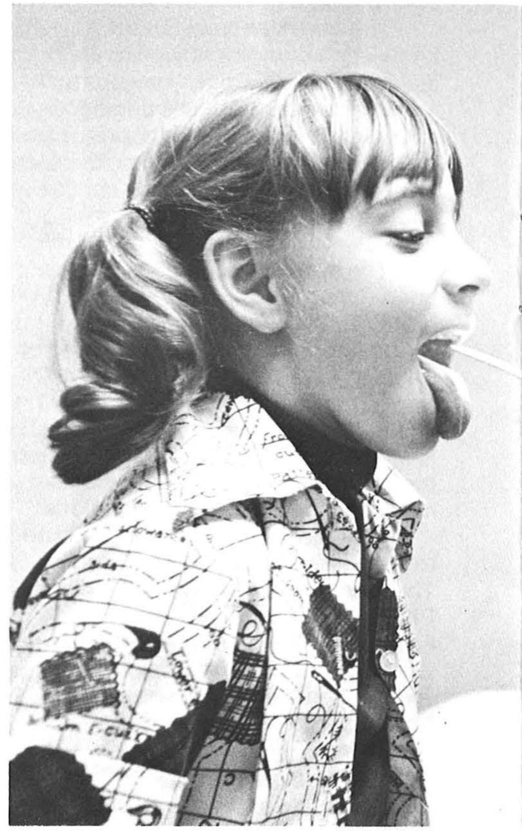
Frozen by liquid nitrogen, cells will stay 'alive' and resume growth in future experiments

Dr. Dennise Richardson works with tiny dishes containing laboratory-grown cells

Dan Barsotti

PAs: Rx for busy MDs

New breed of professional assistants gaining acceptance for their ability to 'extend' doctors' capacity for care



By ANN HARRELL

One approach to the physician shortage in this country is being taken by the UT School of Allied Health Sciences.

While its sister school, Southwestern med, has expanded enrollment in order to double the output of doctors, the School of Allied Health Sciences is training young men and women as physicians' assistants. It is expected that these physicians' assistants in the future will help doctors to provide care for a larger number of patients while improving the quality of care given to those with more serious conditions.

What are physicians' assistants?

The PA, as he or she is usually called for short, is a new breed of health professional. Dr. John W. Schermerhorn, dean of the UT allied health school, describes the role of the PA working with the physicians as "the health professional who relieves the physician of routine duties not requiring the expertise that the physician has developed over the many years of his specialized education and training." In the best sense, he explained, the PA is a "physician extender."

And, according to Dr. Schermerhorn, "We believe the program offered at the Dallas school, which is a component of The University of Texas Health Science Center at Dallas, is one of the best in the country."

A bachelor of science in health care sciences is awarded upon completion of the two-year training course. Currently there are about 40 such degree programs in the U.S.

How do physicians feel about the use of the academically and clinically trained assistants?

John C. Delahunt, USAF retired, is director of the program. He reported that acceptance for the first class of 11, which graduated in August, 1974, was shown by the fact that every one of the PA's was offered positions. During his service years he was a key participant in starting the first PA program in the armed forces.

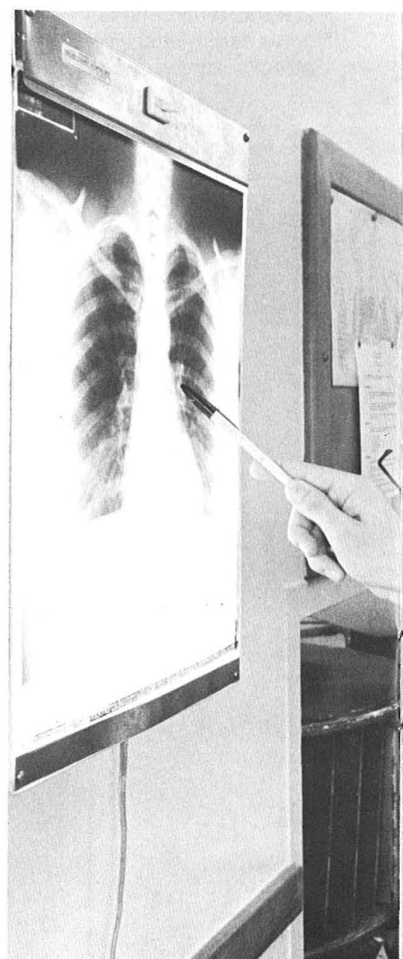
Also, before beginning the program, he said, the School of Allied Health Sciences conducted a survey of 2,584 North Central Texas area physicians to see whether they would accept preceptors for training and/or be interested in hiring program graduates. Over 1,000 replied affirmatively.

One physician in the Dallas area is now singing the praises of the program and the performance of the PA in his office.

"I was not planning to hire a PA when Ms. (Jean) Irwin came to do her preceptorship with me. But she changed my mind," said Dr. Seth Cowan, a family physician in Garland.

"Why? Well, I guess she was a lot more competent than I expected. . . . She was really helpful with routine physicals, and I found her very thorough. After I had her give her first executive physical, I talked with the patient about how he felt about being examined by a PA. He used the same words I have since heard over and over about her from my patients: 'thorough,' 'a good experience' and 'You're lucky to have her'."

What are the duties Dr. Cowan has assigned to Ms. Irwin?



Besides performing physical examinations, she often sees the acutely ill as soon as they come in so she can apprise him of the seriousness of the cases. "Overflow of patients is another area in which I find Ms. Irwin of great help." he continued. "She assists me by sorting my patients out, seeing several and checking on the status of the rooms."

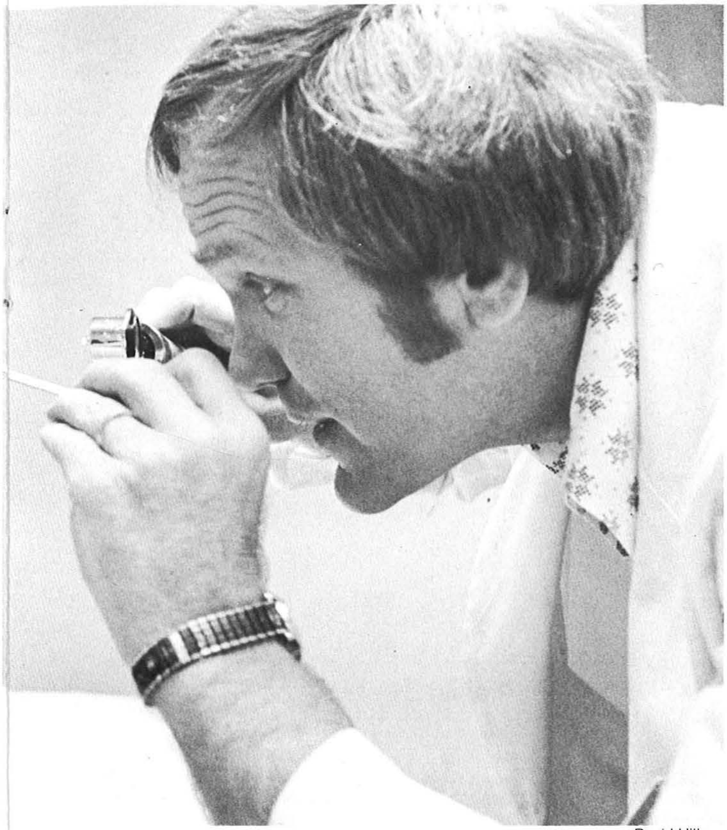
Dr. Cowan said he and Ms. Irwin often make hospital rounds together. Sometimes the doctor makes them alone; other times, if he is needed at the office, he sends his assistant who reports back to him on the condition of the patients.

All duties performed by the PA, however, Dr. Cowan stressed, are done under his supervision and directions.

Another area in which Ms. Irwin assists Dr. Cowan is initially examining and evaluating patients who have upper respiratory infections, ear infections and gynecologic problems. She also sutures minor lacerations, checks newborn babies and pays special attention to the problems of teenage girls.

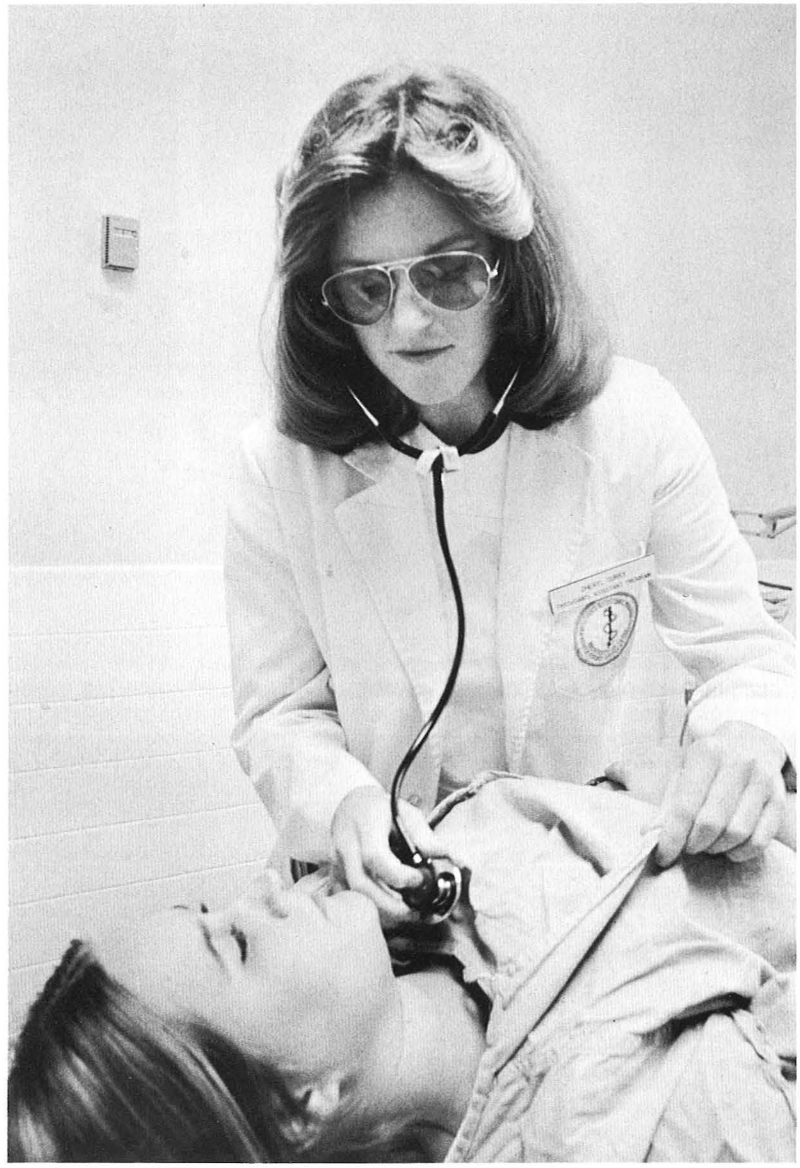
"I have found her especially helpful in answering the questions OB patients have and counseling with new mothers in the hospital about their recovery and child care when they return home," said the M.D.

Ms. Irwin's duties at the clinic have recently been enlarged to include her



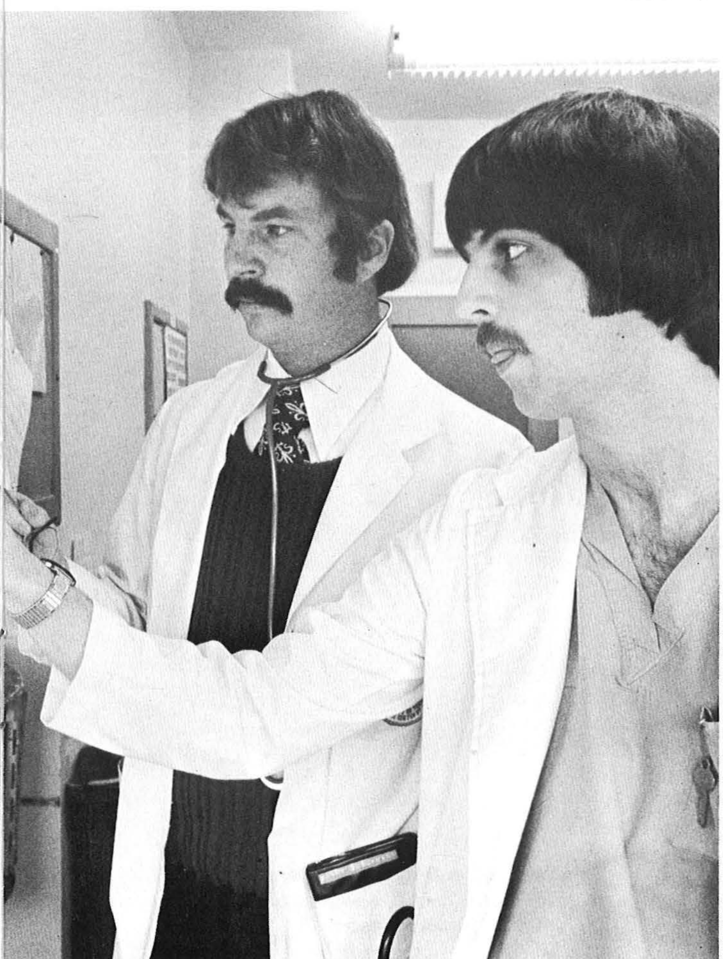
David Hills

**Sheryl Griffin opens wide for Chris Monk,
senior student PA,
during clinical training at Parkland**



David Hills

**Student physician's assistant Cheryl Curry
examines a patient during in-hospital training**



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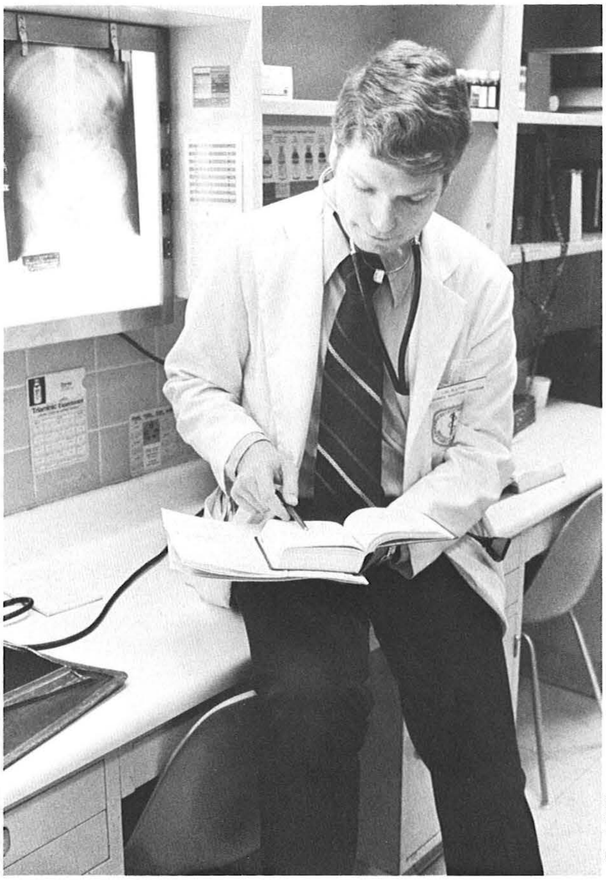
**PA student Garry Fincher (right)
studies X-ray with program coordinator Barry Buschmann**



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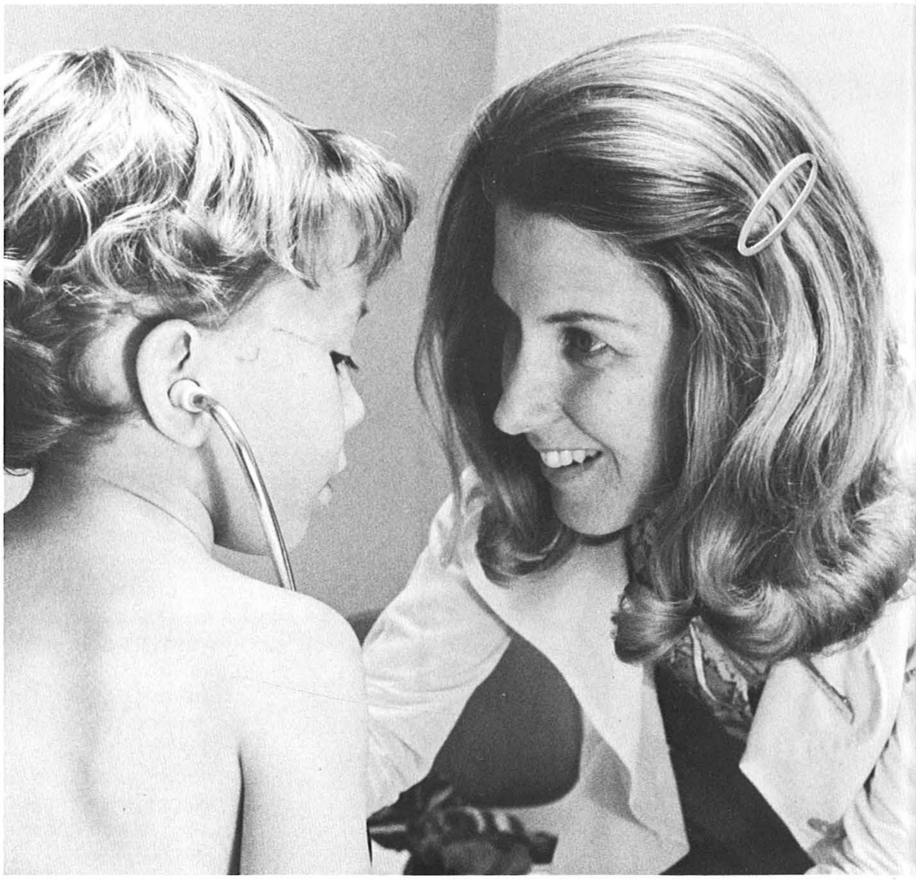
Lou Blettel, PA student, checks a medical reference



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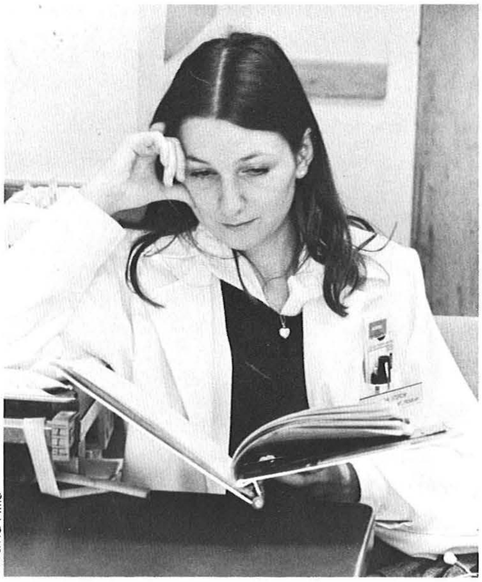
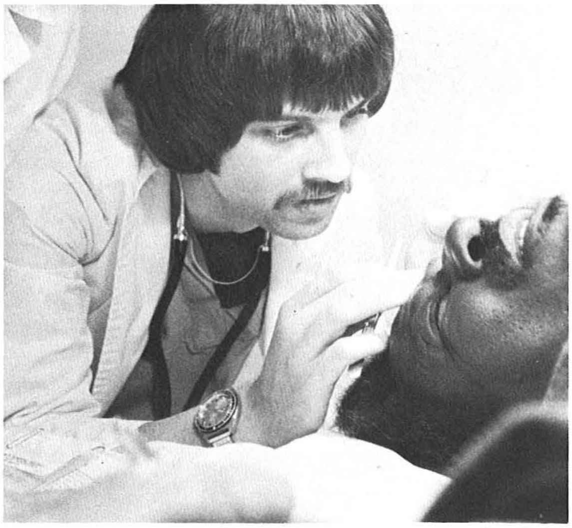
Jean Irwin, graduate PA working in a Garland clinic, lets young patient hear his heart

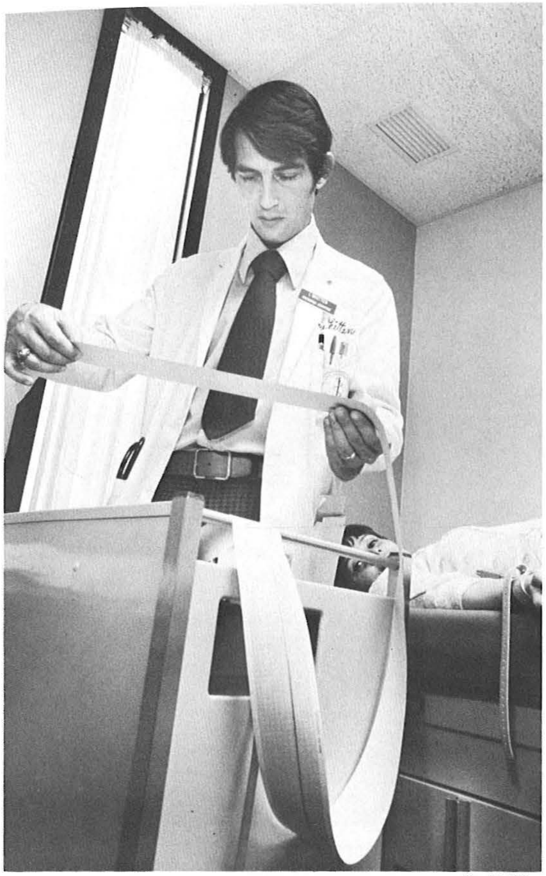


David Hills

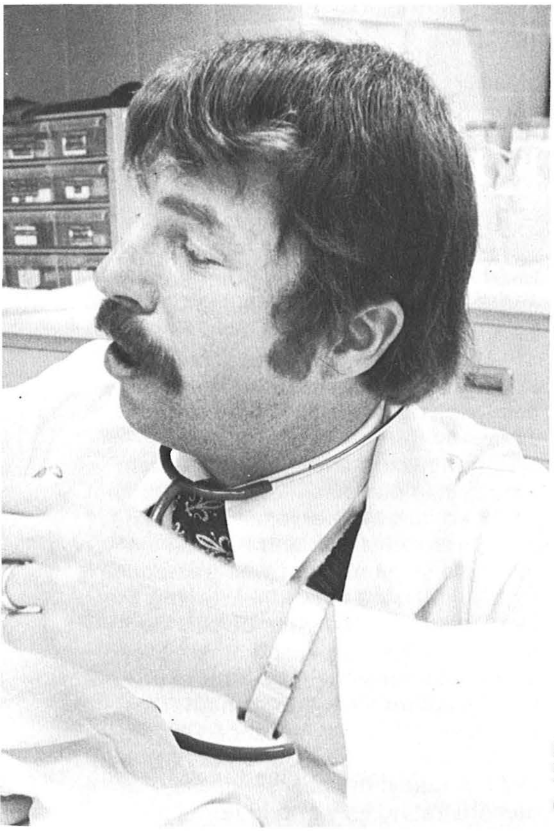
Being a PA student means hours of study



Student Gary Fincher examines patient's eye David Hills



PA Ike Whitten reads EKG in John Peter Smith Hospital clinic, Fort Worth David Hills



David Hills

Program coordinator Buschmann takes time out from teaching to check a young patient

new role as clinical coordinator, an administrative position which also entails the responsibility for directing in-service training among personnel.

She is, he stressed, a "physician extender" in the truest sense. And, Dr. Cowan pointed out, although he had been told that the PA would "pay for himself" in three years, he reported that "Ms. Irwin has paid her way even before the third month of her employment."

As the other graduates of the UT School of Allied Health Sciences' program, Jean Irwin underwent extensive training, both in the classroom and in actual patient-related situations under the direction of physicians.

To enter the UT PA program, a person must have completed 60 semester hours — an equivalent of two years — of accredited liberal arts training in a college or university. Then he or she begins an intensive year-round program.

The first year the PA student studies basic sciences including human anatomy, pathology, physiology, human growth and development, microbiology and pharmacology, both in lectures and in labs at the Health Science Center. The second year, which includes summer sessions, is spent in rotating preceptorships in hospitals, physicians' offices and medical clinics.

"We believe this balance of intensive basic science education with extensive clinical training under the direction of physicians is just the right combination to turn out these highly skilled personnel to assist physicians," Delahunt said.

Currently there are approximately 40 two-year PA programs in the United States.

While working in a clinic in the same suburban city where she lives suits Jean Irwin's needs as a wife, a mother and a professional, Skeet Glatterer, a bachelor, has opted for a more adventurous lifestyle.

Glatterer is one of two physicians' assistants who went to Alaska last December to work as PA's on the pipeline following their graduation. The pair provide the only medical care available for isolated work camps.

These two PA's work under the supervision of doctors who give orders and hold patient conferences via long-distance telephone. Emergencies or acute illnesses that they can't handle are rushed to a major hospital by company planes flown in to evacuate the patient.

"My job in Alaska really isn't as glamorous as it may seem," said Glatterer. Although these two PA's are paid large salaries compared to their classmates and "eat so much steak and lobster I get tired of it," the isolation, the freezing weather, the lack of recreational opportunities and being on call around the clock puts quite a strain on the PA, he pointed out. The company the two work for gives their PA's "R&R" leaves like the military service to help overcome these problems.

Glatterer said that he was surprised how much chronic illness, such as bronchitis, he sees in the camp. "Also, I treat a lot of upper respiratory infections and quite a bit of minor 'stitching up' to do."

"But one thing I never expected on the pipeline was pregnancy problems!" he exclaimed. The young PA was wrong about that, though: one of his first emergencies was when a female clerical worker had a spontaneous abortion.

Still another type of career as a PA has been chosen by Barry Buschmann. Buschmann, also a graduate of the first class at the UT school, joined the faculty of the program on completion of his degree.

"It really worked out well for me. I find I enjoy the teaching much more than I thought I would. . . . and having been in this program myself, I can see how the curriculum can be improved from my own experience. You see, I firmly believe that utilization of this professional, trained by and for physicians, can allow the doctor to spend more of his time seeing, evaluating, diagnosing and treating larger numbers of patients who have more serious conditions than ever before," he stressed.

Buschmann explained that students in the Dallas program are trained to take over a number of routine tasks for the doctor, including taking medical histories, giving physical examinations, performing simple surgical procedures, applying and removing casts and bandages, administering drugs prescribed by the physicians and explaining diagnostic procedures to the patients.

Another way the PA can be of assistance to a physician, he said, is delivering routine services to patients in hospitals and nursing homes or in the patients' own homes. All these duties are, of course, done under the supervision of a physician.

In his role as clinical coordinator, Buschmann acts as liaison between physicians teaching in the clinical year and students-in-training. He also "keeps his hand in" by spending part of his time working as a PA in clinic on a regular basis.

While enthusiastic about the PA program at the Dallas school, Buschmann sees the whole field as exciting. He believes new opportunities will open as more PA's are trained. He is especially excited about PA's bringing medical care to urban communities not being served on a full-time basis by doctors.

"Someday I may want to work in a rural "circuit rider" situation with a doctor myself," he said. ■

the system saves lives


Kurt Wallace/Dallas Times Herald

Crisis: paramedics prepare to 'defibrillate' patient's stricken heart

Using space-age gear, medical school-trained paramedics are providing Dallas with best ambulance service ever

The situation was grim. The patient, a 62-year-old man, had fallen from his chair and lay motionless on the floor.

No pulse. No heartbeat. Breathing had stopped.

"Full arrest!"

Instructions crackled over a radiophone. Quickly, quietly, a team of paramedics from Dallas' Fire Department ambulance service began working over the victim.

With help from a fire engine crew, the paramedics administered cardiopulmonary resuscitation. Following orders from a physician miles away in a communications center at Parkland Memorial Hospital, the team also administered heart-stimulant drugs intravenously and put a tube in the man's throat to help restore breathing.

The closed-chest massage began to work. A weak, wildly irregular heartbeat began. But he could not survive unless a normal beat returned.

The paramedics applied electrodes hooked to portable telemetry equipment, and beamed electronic measurements of the victim's still dangerously abnormal heart rhythm to the Parkland nerve-center. Doctors there read the electrocardiogram readout.

"Defibrillate."

Paramedics R. G. Box and Larry Pierson knew what to do. A portable machine was switched on, and two wired "paddles" were placed on the victim's chest.

Once, twice . . . again and again . . . the electric jolt was applied to the patient. At last, a normal heart rhythm showed on the monitoring screen—after 16 shocks from the defibrillator.

Then, after 35 minutes of feverish activity, the paramedics were ready to move the patient to the hospital. Ten minutes later the ambulance arrived, and the now-stabilized heart victim—who three-quarters of an hour earlier was totally without life signs—was placed in the cardiac intensive care unit in Parkland.

It had been an exhausing, tense struggle. But the medical team had won a touch-and-go battle against death. Ten days later, the patient's damaged heart had mended to the point that he could continue recuperation at his East Dallas home.

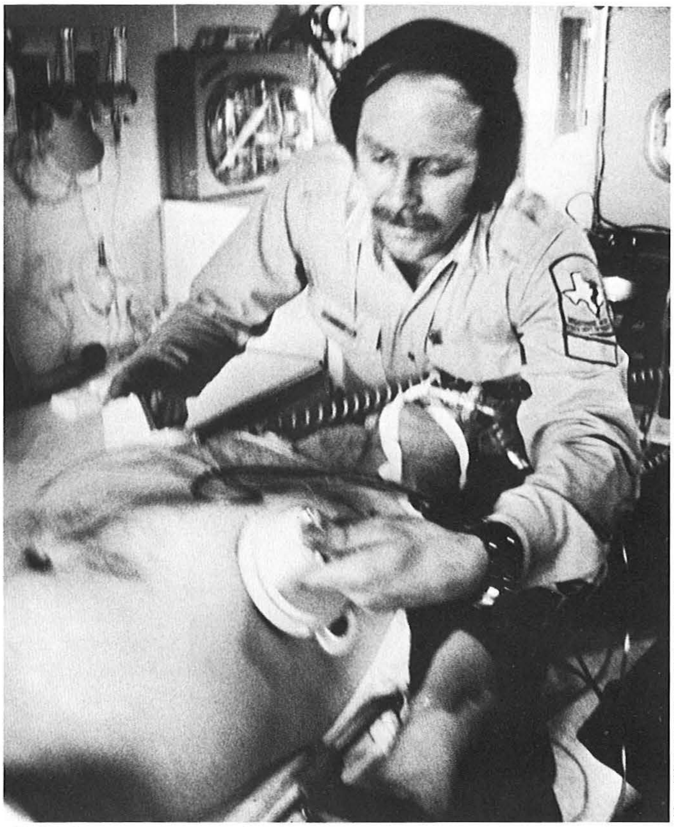
While not always with such a happy ending, similar dramatic episodes are occurring daily in Dallas — and they exemplify the arrival of the best emergency care and transport system the city has ever seen, one which is matched in few other localities.

Paramedics Box and Pierson are part of a small army of well trained, highly motivated personnel staffing the Fire Department ambulance service, which has been providing emergency transportation since November, 1972, and began administering a higher level of service, including advanced cardiopulmonary resuscitation, on Jan. 1, 1975. Already, the new service is demonstrating its worth in terms of improved treatment of severely injured or ill patients during the vital first moments.

"There's no question," says Dr. Ronald C. Jones, acting chairman of surgery at UT Southwestern and chief architect of the paramedic training

Kurt Wallace / Dallas Times Herald

In a race against death, paramedic team wheels victim to ambulance



Kurt Wallace / Dallas Times Herald

Battle's not over: Leon Roddam revives failing heart en route to hospital

Kurt Wallace / Dallas Times Herald

Fire Department's 'hospital-on-wheels' (left) overshadows conventional ambulance

program, "that the new system is saving lives."

"An estimated 375,000 people in the U.S. each year die of heart attacks," noted Dr. Jones. "Some who have been dying are being saved by the earlier administration of proper emergency medical procedures and medication."

Earlier stabilization of the critically ill or injured patient often permits transport at slower speeds, reducing hazards involved in high speed emergency travel.

Emphasizing the importance of prompt, precise emergency measures, Dr. James Atkins, Southwestern cardiologist, points out that 50 to 80 per cent of those who die of heart attacks do so within two to four hours.

"A large number of these patients develop heartbeat irregularities en route to the hospital," he said. Now, techniques and equipment are available to help overcome them.

Not all cardiopulmonary resuscitation efforts by Dallas paramedics are successful, of course. But a study by Dr. Atkins of cases handled during a recent two-week period indicates that the victim of heart attack or critical injury in the city has a better chance than ever before to make it to the hospital alive.

During the study period, 231 patients handled by the city's ambulance fleet required advanced paramedic care. By far the largest single category was heart cases—142. Eighty of these were serious enough to need intravenous medication, and 13 were so severe that their hearts went into ventricular fibrillation—a potentially fatal fast, erratic beat. Paramedics applied the defibrillating shocks to all 13, and three survived to reach the hospital.

In all likelihood, those three patients would have been routine "dead on arrival" statistics before initiation of advanced cardiopulmonary techniques by ambulance personnel, in Dr. Atkins' opinion. A heart specialist in Southwestern's Department of Internal Medicine, Atkins supervised paramedic instruction in cardiopulmonary resuscitation and oversees medical aspects of the ambulance operation on a day-to-day basis.

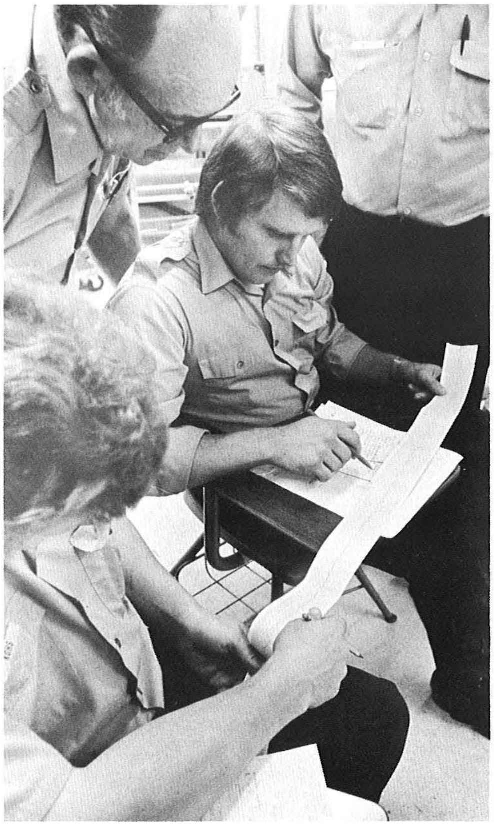
To launch the advanced service, the city of Dallas equipped each of its 16 front-line and six backup ambulances with a $10,000 packet of portable space-age gear, including electronic telemetry for monitoring heart rhythms and sending EKGs, defibrillating device, medications box and portable radio-telephone. (This is in addition to the oxygen, splints and other first-aid equipment already carried.)

Preparing to administer the new techniques, 128 of DFD's emergency medical technicians received 400 hours each of advanced instruction at Southwestern, Parkland and other major Dallas hospitals. This included a virtual "mini-medical school" providing 120 hours of concentrated lectures on a variety of basic medical subjects, given by some 30 members of the Southwestern faculty who volunteered their time for the project. Numerous private physicians also contributed their time.

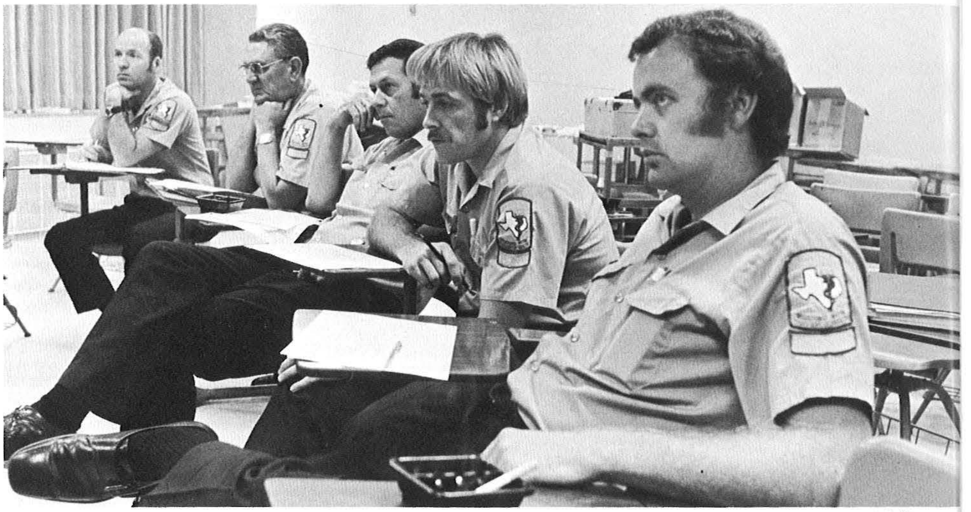
Among subjects taught were obstetrical care, administration of intravenous injections, advanced cardiopulmonary care, treatment of

Paramedics practice heart-shock technique on dummy during training


David Hills


David Hills

Student paramedics examine EKG readout


David Hills

Paramedic trainees are intent listeners during medical lecture, part of 400-hour advanced course

shock due to severe trauma, use of telemetry systems including electrocardiograms. Also, paramedics learned to recognize symptoms of such potentially dangerous conditions as hypoglycemia (low blood sugar) and ketoacidosis (a critical state resulting from excessive blood sugar in diabetes).

Additionally, the advanced paramedics spent 280 hours gaining in-hospital clinical experience during which they worked in coronary care units, labor and delivery rooms, practiced with anesthesia and intravenous therapy, took blood samples, ran and read EKGs and mixed medications. All training was under supervision of physicians and hospital staffs at Parkland, Baylor, Presbyterian, Methodist and St. Paul hospitals.

The advanced classes began in January, 1974, with Dr. Erwin Thal of the Southwestern surgery faculty coordinating the overall effort and Dr. Atkins in charge of cardiopulmonary instruction. Noting the medical school's contribution, Dallas Fire Chief M. C. Hendrix said:

"The city of Dallas would never have been able to meet the cost of training our paramedics without the assistance of The University of Texas Southwestern Medical School and other members of the Dallas medical community."

Under the newly initiated emergency care system, the ambulance paramedics are in constant contact by portable radiophone with specialists in Parkland through a communications nerve-center set up there. The ambulance crews relay patient information including vital signs and, when necessary, send EKG readings by short-wave directly to doctors in Parkland. The physicians in turn interpret this data and instruct the paramedics as to appropriate medical steps, including medication and such emergency procedures as defibrillation.

This new capability places Dallas' emergency ambulance service on a level available in only a handful of other cities —notably Los Angeles, Calif.; Miami, Fla., and Houston. A similar system is being developed in San Antonio.

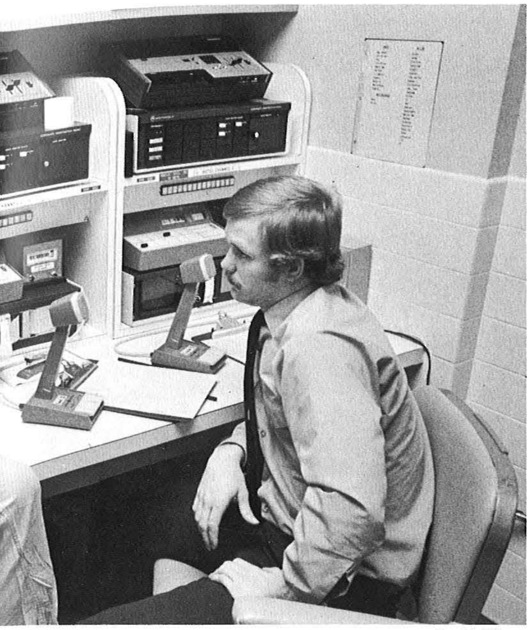
In addition to providing trained personnel and the costly new equipment for each ambulance, the city installed an elaborate radio relay system to make possible instant field-to-hospital two-way communication. The system included seven radio towers to pick up remote signals and relay them via the WRR radio tower at Fair Park to Parkland.

The setup had to be capable of transmitting signals from any far corner of the city, and has even proved powerful enough to send EKG readings to Parkland from within elevators of metal-sheathed downtown office towers.

Although the communications linkup is only with Parkland, fire department ambulances transport emergency patients to any chosen hospital after preliminary emergency care has been provided.

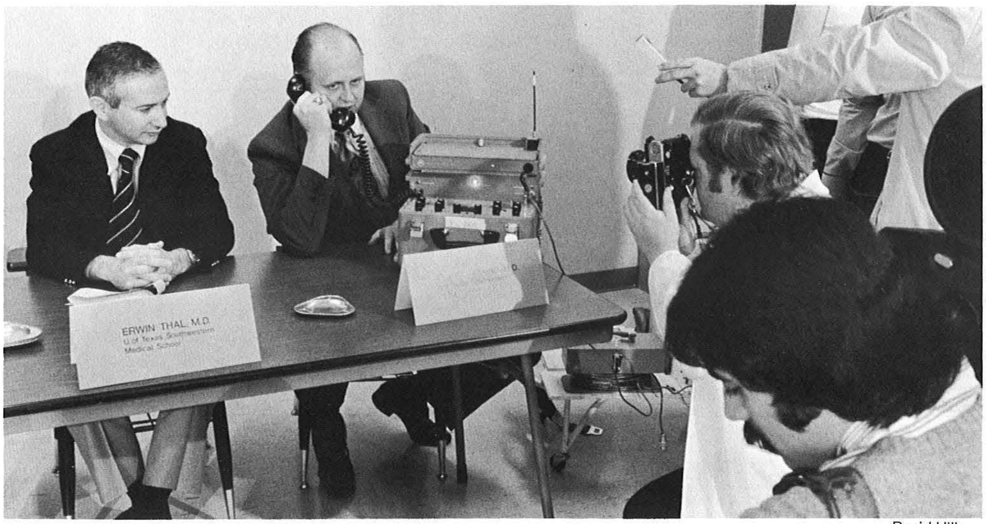
"The paramedics are sufficiently trained to recognize a true emergency and are familiar with emergency services available at each local hospital," said Southwestern's Dr. Ron Jones.

The communications system employs two radio channels plus a dual backup telephone system. Ultimately,



Parkland Physician and Fire Dept. aide confer with ambulance team direct via radiophone

David Hills

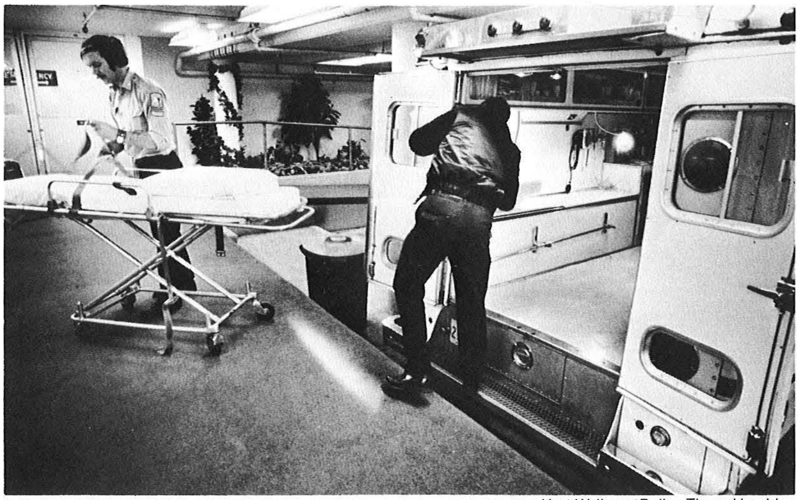


David Hills

Dr. Erwin Thal (left) listens as Dr. James Atkins makes first demonstration call on ambulance radiophone

David Hills

Dr. Ron Jones makes point during media demonstration



Kurt Wallace / Dallas Times Herald

Emergency's over for now, and crew prepares for next call

three more radio channels will be added. In addition to the channels available in Parkland's emergency suite, another remote radio unit has been installed in the cardiopulmonary division of Southwestern, making additional specialists available for emergency consultation with paramedics in the field.

Introduction of the advanced emergency service marks the beginning of a second phase for Dallas' much-praised ambulance operation, which took over from private local carriers in November, 1972. To date some 350 firemen have received basic Emergency Medical Technician (EMT) training, including the 128 who went on to receive the advanced paramedic course. The remainder are available as backup personnel—many of them riding fire engines to help provide additional assistance to the ambulance crews in emergencies.

Last year, DFD ambulances answered 41,246 alarms, bringing to some 93,000 the total calls handled since inception of the service. Initial predictions had projected an annual volume of 30,000 calls. Average response time from 16 strategically located stations has stayed at about four and one-half minutes, despite increased calls. Two additional ambulances have been put into service during weekend peak periods.

Planning and coordination for the new service, including the basic and advanced instruction, was provided by a medical advisory committee headed by Dr. Jones, a recognized trauma expert.

The initial basic EMT course was taught by medical school faculty in 1972. Some 200 firemen received instruction then in closed-chest massage for heart patients, mouth-to-mouth resuscitation, installation of throat airways, immobilization of fractures and spinal injuries, childbirth, burns care and other types of emergency treatment.

Now, a few months after beginning the more advanced level of service, it is apparent to emergency room doctors and hospital personnel that the system is working well. Far more severely ill or injured persons are reaching the hospital with stable vital signs.

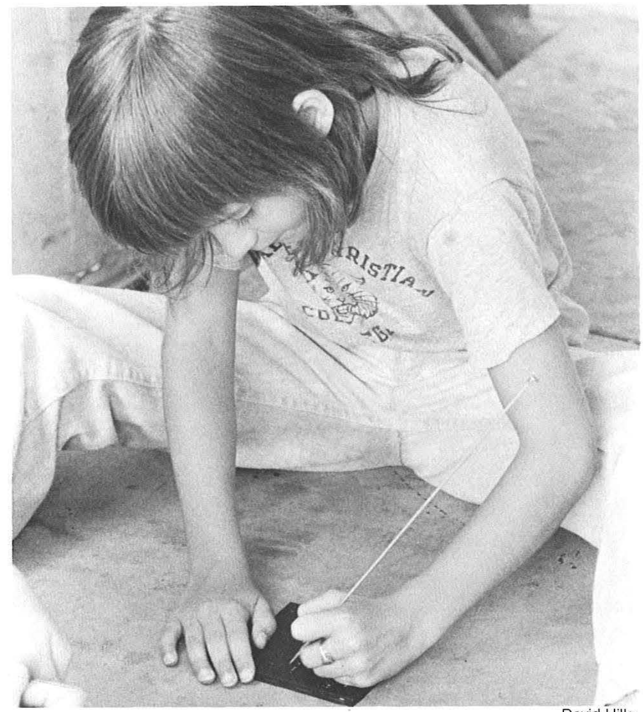
Division Chief Bill Roberts, who heads the fire department's ambulance operation, and has been involved in developing the service since 1969, sets a high goal:

"We are attempting to build the best emergency care system in the world," he says, "and we've just about achieved that."

A growing number of patients—certainly including a 62-year-old Dallasite who survived a brush with death because of the paramedics' skill—heartily agree. ■

—JOHN WEEKS

Healed Hearts get Healthy Workout



David Hills

Betsy Bennett enjoys crafts at the exercise camp

David Hills

Who knows? One of these 'heart campers' may end up in medicine herself.

David Hills

Dr. Damaris Young checks blood pressure while young patient pedals

David Hills

Betsy proudly raises her hand to ask 'her doctor' a question when Dr. Miller visits her class

Testing's tiring—but swimming fun follows workout

Neal Pointer

Patient wears 'space helmet' during final testing by Dr. Miller in Southwestern lab

"You all know Betsy Bennett. And you know Betsy Bennett is as normal as any of you," said the smiling man with the beard to the assembled classes of third grade boys and girls sitting at his feet as if for a story hour.

The scene is David Elementary School in Plano, the man is Dr. William W. Miller, associate professor of pediatrics at UT Southwestern Medical School. He is Betsy's doctor and visiting her classmates at her request. Besides telling the youngsters about their hearts and how to keep them as healthy as possible, the physician told the group about Betsy—who, although a cardiac patient, is as normal as they, he stressed—and her friends who participated in a special kind of day camp last summer.

In the summertime thousands of boys and girls in the Dallas Metropolitan area are joining in bike rides, swimming parties, lake fun and soccer and sandlot ball. But there is one child who sometimes has been left out of these vacation pleasures—the child with a heart defect. "Although many studies have been done on exercise and adults with these problems, none had been done on children," he said.

So last summer Dr. Miller and his associate Dr. Damaris Young put 15 youngsters through a five-week program of exercise to determine the effects of exercise on the hearts of children who have previously undergone serious heart surgery. To make it a vacation treat, the training was done during the hours when daycamping is a popular pastime with kids. The kids worked out on exercycles in the Town North YMCA, which proved a perfect place for the "day camp." Not only did the program involve swimming in the Y pool, but there were active games, gym session and arts-and-crafts time.

At the end of the five weeks, the boys and girls took their "finals" at Southwestern's Weinberger laboratories checking cardiopulmonary function, blood pressure and changes in lean body mass.

Further studies will have to be made to determine if longer training periods are needed for increased capacity. But both they and their parents proved that the kids can have fun exercising like their friends and taking part safely in athletic programs in school.

As Dr. Miller said, "You know Betsy Bennett. And you know Betsy Bennett is just as normal as any of you." ■

—ANN HARRELL

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