

Health Science Spectrum



Science writes happy ending for postponed pregnancies

The president's message : Reordering priorities for the Eighties

During the Sixties and early Seventies, a fundamental goal of medical education was to carry out a public-policy mandate to expand teaching capacity sharply in order to overcome a severe national shortage of physicians. Existing schools did indeed expand, many new ones were established, and the number of annual medical graduates nationally leaped from 8,000 in 1963 to more than 15,000 in 1978. In this period The University of Texas Southwestern Medical School approximately doubled its medical enrollment, from 420 to 823. Statewide, the number of medical schools increased from three to eight.

Now, national perceptions and priorities are again changing — and just as dramatically as before. The growth rate of medical enrollments has slowed drastically, signaling that the expansionist period is at an end. In fact, we might not just apply the brakes, we may even shift into reverse — for there is a substantial body of opinion that the expansion of medical education viewed as so necessary in the Sixties, coupled with an increasing inflow of foreign medical graduates, may produce an oversupply of physicians during the Eighties. Secretary of Health, Education and Welfare Joseph Califano recently suggested that medical colleges — which were being encouraged (and rewarded) to enlarge their classes a decade ago — should now begin to consider trimming student rolls.

So at the very least, a plateau has been reached, and an important reassessment is under way.

In Texas, the medical manpower picture remains clouded by nagging problems that continue to evade satisfactory solution: a geographic maldistribution of the available doctors, and a persistent shortage of those



engaged in "primary care" — general medicine, family practice and pediatrics. Moreover, the physician-to-patient ratio remains unfavorable, according to 1976 estimates which show Texas lagging behind with 134 doctors of medicine for approximately every 100,000 residents, compared to a national average of 163 for each 100,000 citizens.

So questions remain — and today's inflation-wracked climate demands cost-effective answers. In my view, two paths of action open to policymakers in Texas promise to be both effective and efficient:

First, recent studies indicate a far less expensive and potentially more productive means of overcoming much of the remaining physician shortage in the state is available through the expansion of residency training programs in Texas medical teaching hospitals. A recent survey of Southwestern graduates showed graphically that it is the place of residency — rather than the site of medi-

cal schooling — that is the predominant factor in a new doctor's ultimate choice of location. This study, published in *Texas Medicine*, turned up some startling figures: among native Texan graduates of Southwestern, 82 percent of those who took residencies in the state stayed here to practice — compared to only 34 percent of those Texas-born students who went to other states for graduate training. Even among Southwestern graduates originally from out-of-state, 73 percent who pursued residency training in Texas remained here, while only 22 percent of the same group returned after going elsewhere for graduate training.

Thus increasing residency training positions in Texas, to approximately equal the number of annual medical graduates, appears to be an efficacious answer to the state's shortage of physicians. Out-of-pocket expenses for resident training are only a fraction of the cost of undergraduate medical education, so increased support for residencies would almost certainly accomplish more, with less, than any further building of medical school capacity.

And by placing emphasis, in these newly created residency positions, on training in those needed primary-care disciplines, the process could be steered toward correcting the professional imbalance that remains — and, because opportunities to practice in those disciplines lie heavily in medically underserved areas, the geographic imbalance could be ameliorated as well.

A second step, one that would help facilitate the first, would be enactment of pending legislation to give needed financial assistance to Texas' primary medical teaching hospitals — such as our own partner, Parkland Memorial Hospital. The state needs to recognize,

Health Science Spectrum

The University of Texas Health Science Center at Dallas

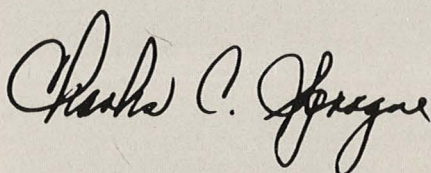
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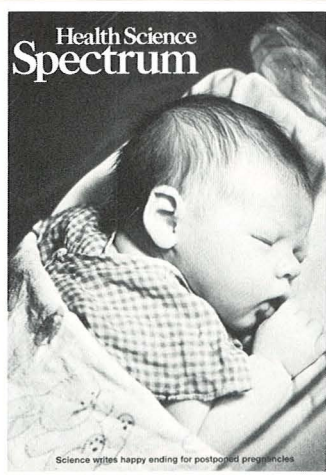
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and correct, the inequity that exists between the larger counties that provide the tax support for this vital portion of the total medical-education process, and those counties that do not.

Besides being equitable, this action would be pragmatic. The communities which under this legislation would start sharing the cost of graduate medical training are the very ones most likely to benefit from the state's resulting increased ability to attract and retain additional practitioners, mostly in primary care. And this comparatively modest investment would help move Texas ahead in the 1980s toward meeting realistic, readjusted goals for improving its health services.



Charles C. Sprague, M.D.
President



On the cover: In 1979, the International Year of the Child, medical advances reduce the risks accompanying pregnancy for mothers over 35. This newborn at Parkland Memorial Hospital shows the happy results. Photograph by Darryl Baird.

Saving Babies

**Life-giving advances
are easing risks associated
with delayed pregnancies**

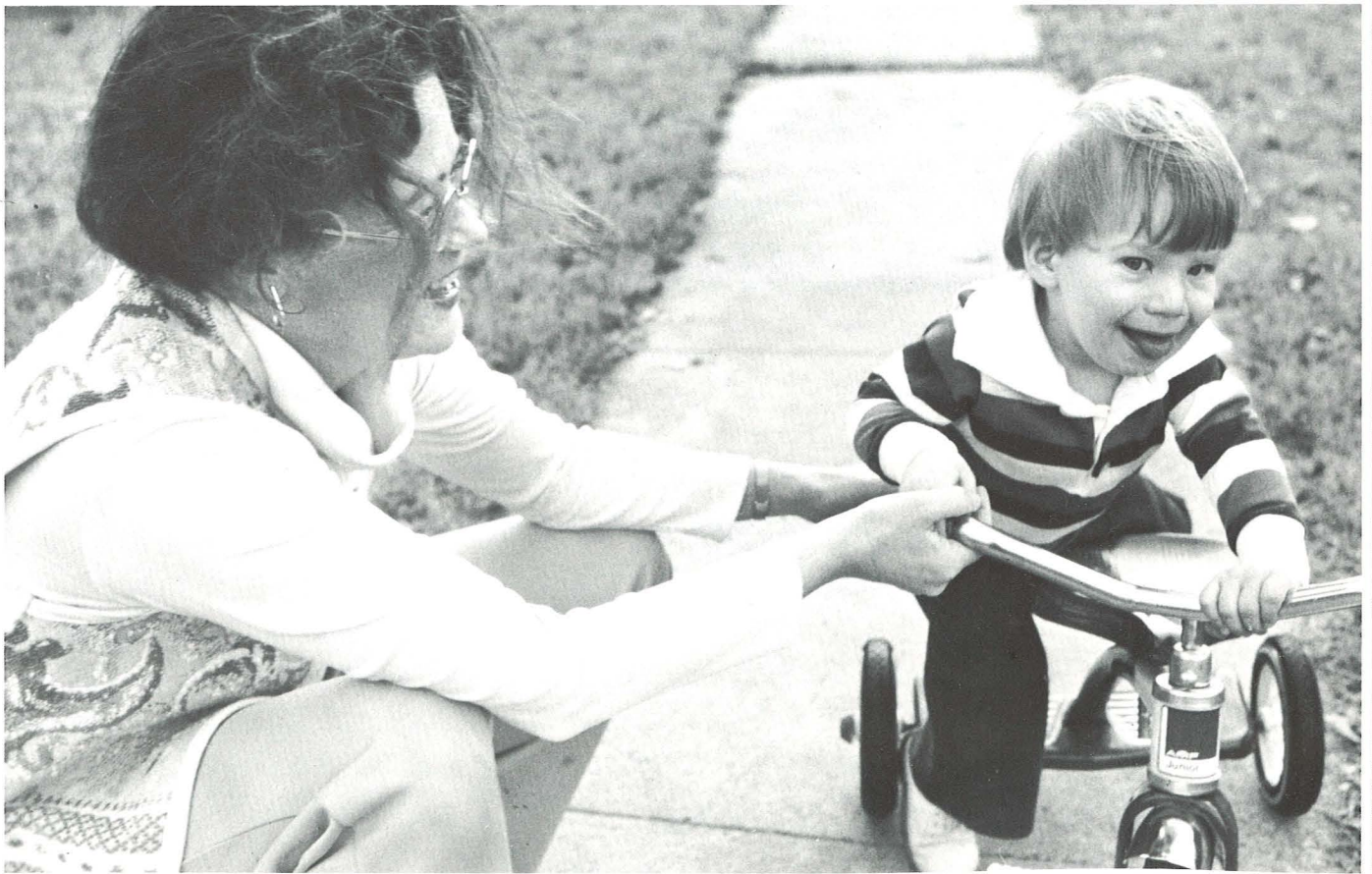
By Ann Harrell

Photography by Darryl Baird

Fletcher is no ordinary baby — he is the child his mother thought she would never have.

“Prenatal testing gave me the courage,” says Fletcher’s mother, Marcia Purdy, or Marcia Schramm, as she is known professionally. This mother is one of the growing number of women, mostly middle-class, urban and established in their careers, who are part of a trend toward delayed pregnancies. First-time mothers in their late thirties — and even in their forties — are no longer rare.

Marcia was 44 when she had Fletcher. A native of Iowa, she had come to Dallas to start the graduate program in dance at Southern Methodist University five years ago. Here she met and married Hareld Purdy, “a very gentle, very honest man.” Hareld was already the father of three children in their late teens and twenties. Nevertheless, both Purdys wanted to bring a child into



their new home.

Both, too, were aware of the possible dangers, both to mother and child, of pregnancies in women of advanced child-bearing age. More prevalent in older women are maternal complications such as high blood pressure and kidney problems. Babies born to these mothers have a higher incidence of certain congenital disorders. Some of these are chromosomal disorders like Down's syndrome (formerly called mongolism) and neural tube defects like spina bifida (open spine).

In 1970, it was estimated that 13 percent of pregnancies in women over 35 resulted in 50 percent of the infants born with Down's syndrome. According to *The New England Journal of Medicine*, one woman in 800 bears an infant with this genetic disease; the incidence rises to one in 300 at 35 and to one in 50 at age 40.

Amniocentesis (drawing amniotic fluid from the fetal sac) is being recommended more and more to women like Marcia Purdy as well as those aware of a family history of genetic diseases. Also, patients who are already parents of one handicapped child are being encouraged to have genetic counseling and amniocentesis as well.

One of the few places in the North Texas area where this kind of amniocentesis is routinely performed is The University of Texas Health Science Center through its Dallas Regional Perinatal Program.

Funded by the Robert Wood Johnson Foundation and supplemented by grants from Health, Education and Welfare, these regional programs are located in only four states. All resources of the perinatal team are aimed at identifying, evaluating and treating high-risk pregnancies. The Dallas center is one of the national forerunners in medical care to both mother and child.

Amniocentesis has been used at the center since 1970 to check the maturity of the fetus' lungs or kidneys and to detect and treat Rh incompatibility problems at a late stage of the pregnancy. In 1972, earlier amniocentesis for prenatal diagnosis of genetic problems became a part of the perinatal program, which offers services to all private physicians, as well as to the center's teaching hospitals.

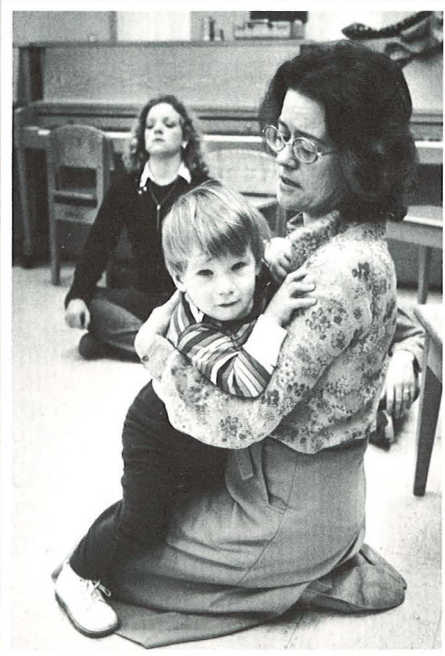
Relatively painless, the procedure, including sonography, takes less than an hour. The location chosen for insertion is deadened with a local anesthetic. Most patients report, at

most, a sharp cramp as the needle enters or a sensation much like a gas pain. Last year 154 amniocenteses were performed on patients from a large area of the state. Here scientific advances, such as amniocentesis, genetic counseling, sonography and high-risk care of both mothers and newborns, are allowing more wanted babies to be born to mothers over 35.

Women of today who postpone having children for economic and professional reasons might never have conceived a child or would have aborted a pregnancy due to fear of age-related birth defects. Thus amniocentesis is truly a life-giving process.

"We are able to give our patients information on which to base real choices about continuing or terminating a pregnancy, and it is very reassuring to them during the remainder of their pregnancies," says Dr. Norman Gant, chairman of Obstetrics and Gynecology at the health science center.

Dr. Stuart Stone, a Dallas obstetrician, says he has seen no increase



Fletcher joins the fun in one of his mother's movement classes at SMU's Meadows School of Fine Arts. Observing his stages of development is a bonus for the dance students, many of whom plan to be teachers.

in abortions due to amniocentesis. In fact, he says, the number has remained constant since abortion for non-medical reasons became legal.

Not all patients who are given a negative report on their amniocenteses choose to terminate their pregnancies. Stone says some, especially those who know they are greater risks because of their genetic histories, want amniocentesis. "These patients say they want to know so they can 'get their heads' ready in case the test shows they will have a handicapped child."

However, Stone warns that amniocentesis should not be viewed as a panacea. "It's unfortunate laymen have too often gotten the idea that you just plug in the (amniotic) fluid for the test and everything will be fine."

There are risks. No matter how carefully done, bleeding or leakage of amniotic fluid from the fetal sac may lead to miscarriage. If the placenta is injured, an Rh-incompatibility reaction may be triggered.

Nor is the test perfect. In a study reported in *The New England Journal*, there were 14 diagnostic errors in 3,000 procedures, six serious enough to affect the parents' decisions about whether to abort or give birth. Either parent may be a



This sonogram shows the healthy fetus of an over-35 mother.

"carrier" of Down's syndrome, but there is no test for a male.

Before performing amniocentesis for genetic problems, genetic counselors Dr. Mary Jo Harrod and Dr. Jan Friedman explain the procedure and its risks and interpret the chances of having a handicapped child on an individual basis to each patient. They also explain that in a few instances the test must be repeated if cells fail to grow in culture. The whole prenatal-testing procedure, including sonography (picture

of the fetus by ultrasound), costs around \$450. Charges for more complicated and unusual genetic tests are not included.

Testing is offered to all patients who see faculty members and residents at the center and its teaching hospitals. At present about one-half of the physicians seeing obstetrical patients in the Dallas area refer appropriate patients to the center for these prenatal services. The geneticists agree that there will be an increase in the number of referrals in the future because of a January, 1979, court decision. The New York Court of Appeals has held physicians liable for additional medical costs because they did not warn the prospective parents of possible higher-than-usual risks for defects in their offspring.

This kind of accurate information is what the UT genetic counselors strive to provide. It is upon this information and the genetic interpretations made by the counselors that each set of parents must base their joint decisions. "We never tell a couple what to do or what not to do," says Harrod. "We explain the possibilities and chances and let them decide."

The culture from the amniotic fluid will tell whether the child is male or female. But Friedman and Harrod stress that sex determination is not considered an appropriate reason for prenatal diagnosis except in cases of sex-linked disorders like hemophilia. Sometimes the counselors may refer a couple for artificial insemination in certain cases of sex-linked genetic disorders.

Physicians at the center believe that amniocentesis is best accompanied by sonography, a painless procedure which translates echoes into shapes on a TV-like screen. Sonography is used to gain information about the pregnancy in order to avoid injuring either the fetus itself or the placenta during amniocentesis. Dr. Rigoberto Santos-Ramos, the center's sonography expert, also performs sonography for other medical reasons.

Women with special medical problems during pregnancy need spe-



Amniocentesis for prenatal diagnosis of genetic problems became a part of the health science center's perinatal program in 1972.

cial care. Dr. Peggy Whalley, professor of obstetrics and gynecology, established one of the early wards for "high-risk" mothers at Parkland Memorial Hospital in 1973 in order to head off major complications to both mother and child. She started a second high-risk program at nearby St. Paul Hospital this year. Patients in these centers average two-month stays.

Among problems that bring women to a high-risk ward are high blood pressure, which can cause convulsions and result in kidney damage, and diabetes, which is often accompanied by circulatory problems. These conditions are not only dangerous to the mother but also to the fetus. And both can lead to premature delivery, the single largest cause of infant death in the U.S.

Major advances in both perinatal and neonatal care have lowered the neonatal mortality rate as a whole in this country. A great deal of credit for saving newborn lives in Dallas, says center neonatologist Dr. Charles Rosenfeld, goes to the obstetricians aware of high-risk pregnancies and the availability of more neonatal and pediatric intensive care units. These units are not only saving infants' lives, but producing healthier babies. There, highly specialized equipment with highly trained staffs are key to the premature infant's survival.

What happens to parents like Marcia and Hareld Purdy if after going through counseling and prenatal testing, they were to have a severely handicapped child? Are they left to deal with the problems of the child and resulting problems to the family alone?

No, says Dr. Doman Keele, associate professor of pediatrics, who heads the University Affiliated Center and acts as assistant director for the Birth Defects Center at Children's Medical Center. The two centers offer services to these parents which include immediate consultation, medical evaluation and follow-up by the birth defects team and other specialists; genetic counseling for parents; referrals to local agencies where parents can find help and support; and "crash cour-

ses" at the University Affiliated Center, a training program for health professionals who will be working with handicapped children.

"Grief counseling is also offered to these parents, for often when a child with a birth defect is born, the parents go through exactly the same stages of grief as for a death. But through counseling, parents find that having a handicapped child is not the 'end of the world.'

"There is a great variability in the severity of many handicaps," Keele points out. And some handicaps are slight and treatable, such as cleft palate and clubfoot. A few disorders may even be treated *in utero* during

the mother's pregnancy. Also, there are many degrees of severity in the mentally retarded child, and many of these children bring joy to their families and function well as adults.

Marcia agrees. Fletcher was born with a clubfoot, one of the defects that do not show up with prenatal testing. His problem, however, is slight and is being corrected by a special brace and exercise.

"It's a small price to pay for the child I thought I would never have. And wouldn't you know a dancer would have a baby with a clubfoot?" she adds with an impish grin. ■



Both Marcia and Hareld enjoy spending a lot of time with Fletcher.

Maelstrom of mistreatment

Despite myths of universal love, child abuse and neglect constitute a national disgrace.

For many children "Hansel and Gretel" is no fairy tale.

Not even in "America the Beautiful" where social myth proclaims that, above all, our country loves its children. Actually, there are one million cases of neglect and abuse to children each year. And those are only the reported cases. Many believe the known statistics reflect only a shadow of the true picture.

In an effort to stem this mistreatment, the National Center on Child Abuse and Neglect has designated four national demonstration programs, one involving the successful Children and Youth Project conducted here by the The University of Texas Health Science Center at Dallas. The C&Y Project, which uses a team approach to deliver health care to more than 13,500 infants, children and adolescents in impoverished areas including West Dallas, is in a strategic position to implement the new program.

In spite of previous efforts by the National Center and the American Humane Association to determine the true magnitude of the problem, no one has a clear idea of the number of children who are maltreated.

Juvenile officials and welfare agencies estimate there is probably 10 to 20 times more abuse and neglect than is reported. Of the totals which are reported, 800,000 cases a year involve neglect, while abuse, which usually gets more publicity, accounts for 200,000 cases.

In Dallas, where one mother has been charged with murder after one of her emaciated twins died of starvation, statistics show far more abuse than neglect (although reporting methods differ from national practices). For 1977, the last available year, known cases of maltreatment totaled 7,106, according to the Texas Department of Human Resources. The department says that figure, however, is probably low.

In fact, according to a report recently released by the Criminal Justice Center at Sam Houston State University, figures for abused and neglected children under 15 may run from 283,000 to 400,000 in the state. And while these modern-day statistics are disturbing, it must be remembered that the problem is not new.

Psychologist David Bakan says evidences of the universality of child abuse and neglect may be readily seen in our culture.

Bakan, of Toronto's York University, points out that in fairy tales like "Hansel and Gretel," it's the wicked stepmother, rather than the mother, who is cruel to the children. The reason, he says, is because a natural mother's mistreatment of her children is too psychologically devastating for us to deal with. He also points out that many children taken to emergency rooms because of "accidents" in the home call to mind a familiar refrain for most of us from childhood:

*Rock-a-bye, baby in the treetop,
When the wind blows the cradle will rock;
When the bough breaks the cradle will fall.
Down will come baby, cradle and all.*

Most Americans would be shocked to learn that the first recorded intervention in a child-abuse case had to be brought under the auspices of the Society for the Prevention of Cruelty to Animals because there were no laws in 1874 to protect our children from their parents' complete control. And it was not until 1946, with increased use of X-rays in medicine that physicians began to realize that children with a wide assortment of broken bones and hematomas (tumors with excessive blood) over a period of time were suffering from physical trauma, not an obscure disease. In 1961, Dr. C. Henry Kempe, a pioneer physician in combating the maltreatment of children, coined the term "battered-child syndrome" to describe this condition.

Like Humpty Dumpty some of these children cannot be "put together again." Hoping to intervene in cases of neglect and abuse before the child "falls," however, the Department of Pediatrics at the Dallas health science center has initiated two programs with different approaches to identifying and attacking these problems.

One expands the medical care already offered to the pediatric population of an area with the lowest per capita income in the city. C&Y Project services will include an

intensive effort at ending child neglect and abuse. The other program offers diagnostic and on-going medical services to abused and neglected children through special clinics and emergency room services at the county hospital.

A grant of \$129,732 will be used in the four C&Y clinics to deal with child neglect. The four programs nationwide are the result of first-time federal grants in the area of neglect.

Goal for the C&Y Project, funded primarily by the Department of Health, Education and Welfare, is to produce a generation of healthy children, says Dr. Heinz Eichenwald, chairman of the Department of Pediatrics. And statistics compiled by Dr. Thomas Moore, director of the project, show that in the seven years since the C&Y clinics opened, hospitalizations and deaths among children who see these health teams for medical care have dropped significantly.

Each health team includes a pediatrician, nurses, social workers, a dentist, dental personnel and a clinical psychologist. Services of a nutritionist and a physical therapist are shared. Because of the ethnic makeup of the community, one health team is completely bilingual. The other three have some staff members who are Spanish-speaking.

Because of the close relationships the health teams develop with the families who bring their children to the neighborhood clinics, the C&Y teams are in a unique position to work with neglecting families. Says Aileen Edgington, supervisor of the social workers and principal investigator for the grant, "Members of the health teams become aware very early of patterns of neglect in a family, of the babies who are 'at risk' because of failure to thrive, physical and emotional neglect and, of course, abuse."



"Early tomorrow morning we will take the children out into the forest to where it is the thickest. There we will light a fire for them and give each of them a piece of bread more. Then we will go to our work and leave them alone. They will not find the way home, and we shall be rid of them."

Hansel and Gretel

A social psychotherapist, Edgington feels that the successes the C&Y program has already had with developing individualized treatment plans for many families with children "at risk" was a major reason the Dallas project received the grant. These treatment plans may include developing parenting skills, nutrition education, day-care arrangements, psychotherapy appointments, helping parents find employment, financial management counseling and health care for parents. Team members are currently working with 120 cases of severe neglect.

How does the team identify what the workers call "at risk" cases? Edgington says that clues to severe neglect situations often center around the mother because in most cases she will be principally responsible for caring for the child: Is the mother unusually young, immature, resentful of the child's interference with her activities, especially shy, uneducated or still in school, unskilled, retarded or handicapped? Has she been in trouble at school or with the law? Is she married? Does she have a family

“Everybody gets excited when babies are growing — the mothers and the staff alike. So we give mothers lots of ‘strokes’ around here.”

that is emotionally supportive? Does she have an adequate place to live and money to feed herself and the infant? Is she healthy and did she have good nutrition and medical care during her pregnancy?

Dr. Paul LaPorte, C&Y pediatrician who has been with the health teams since their beginning, believes that most of the mothers he sees *want* to be good mothers. Edgington agrees. “Everybody gets excited when babies are growing — the mothers and the staff alike. So we give mothers lots of ‘strokes’ around here.”

Many, however, do not know how to be mothers at all. Too often they are literally children themselves. That is why, LaPorte says, the team nurses try to make home visits within 48 hours after the mothers are released from the hospital with their babies. Referrals are made during the hospital stay.

“If the social workers find a high-risk situation in the home, then they try to get the mother to bring the baby right in so we can follow it closely,” the physician says. “Otherwise, the social worker encourages the mother to bring the baby in for a new-baby check-up in two to four weeks.”

One of the most frequent evidences of neglect seen in the clinics is failure to thrive. When the baby is not gaining weight as it should, often the mother needs child-care instruction of the most basic kind. Then if the baby still doesn’t “catch up,” staff members encourage her to let the baby attend a nearby 24-hour child-care facility with which the program contracts. Removal from the home for longer periods is sometimes necessary because proper nutrition is of primary importance in infants and young children to avoid brain damage.

Besides the immature parent, who is often a very young teen-ager, there is another kind of immaturity associated with neglect, says Norman Polansky, national leader in the field. The “impulsive” mother may disappear from time to time on sexual adventures. The “impulsive” father may take off on alcoholic binges. Many of these parents are attentive most of the time, Polansky says.

In many cases neglectful or abusive parents come from homes in which they themselves were maltreated. There are also many examples of parents who seem so steeped in apathy and futility that even the most aggressive attempts by professionals many times cannot reach them.

Some parents may be chronic alcoholics, drug addicts or habitual criminals. Some seem to have absolutely no empathy with their children, and some are emotionally ill themselves. There also seems to be some evidence that unwanted pregnancies may be a factor, as well as failure of the mother and child to form a bond between them, especially if the child were kept in the critical-care nursery for a long period of time after birth.

Many were abandoned as children themselves. There is also evidence that “role reversal” (the parent’s expecting the child to love and take care of him or her) is a factor. Also, isolation from the community may reinforce feelings of frustration and lead to further withdrawal.

Although there are many cases of child neglect and child abuse among poverty-level people, there has been no evidence that poverty in itself causes either neglect or abuse. Poverty, however, does place additional stress on a family.

Problems like these are where team cooperation makes all the difference, LaPorte explains. “We follow these cases on a regular, confidential basis in our weekly staff meetings so we can share opinions, get different ideas and set priorities. Some of the cases are complex — they’ve got some social, some nutritional and some psychological problems all mixed together. If you don’t go at the whole ball game, you lose them.”

When a team member becomes suspicious of neglect or abuse, he or she brings it to the attention of the whole health team. Some of these clues to maltreatment include dirty children, improper clothing, lice, infected bug bites, broken bones, bruises, absences from school, emotional withdrawal and venereal disease (from sexual abuse). Teachers often send enrolled children to the health team when they suspect something is wrong, and welfare workers, with whom the team coordinates closely, may also contact the clinics. It is not unusual for neighbors or relatives who care about a child to call maltreatment to the attention of the health personnel.

“Throwaway” children, those who have been abandoned by parents, and teen-agers who have often been kicked out to fend for themselves are another kind of neglect problem in the neighborhoods. They need help, too. Often these teens, and even younger children, simply float around the area, living with one relative or neighbor, then another. One West Dallas teen-ager — who had a baby herself — was found to be living under a tree.

Often “at risk” families are already under review by child welfare. Some do, unfortunately, end up in court. It is estimated that 150,000 child-neglect proceedings are heard yearly in the U.S. Sometimes options such as foster or institutional care or, better yet, placement with a relative, must be sought for the good of the child. Edgington believes that, whenever possible, the team should continue working with the family with the return of the child as the end-goal. Also, it is always better when placements can be made on a voluntary basis. Family therapy may be necessary

before the child's return, as well as later.

Cheryl Phillips agrees that these decisions are difficult.

Phillips is a social worker under medical director Dr. Roy Heyne in a child-abuse and neglect program at Children's Medical Center and the Dallas County Mental Health and Mental Retardation Center's Referral and Evaluation for Abused Children (REACH) program. MHMR has contracted with Heyne and the health science center to offer medical and psychological services to abused and neglected children.

"Frequently there is no *best* way," the social worker says. "You have to come down from your ivory tower and realize whatever happens is going to be damaging to the child. You look for the least damaging alternative."

Phillips says that often removing a child from a family creates new problems. Another child may be selected for the scapegoat role. Or a family "seals up." Members learn to go about their daily lives without the missing child until he or she may not be missed. Thus when a child is returned to the family he or she may be literally an outsider.

Heyne and Phillips, who work as a team, deal with these and other tough questions daily.

The pediatrician, a part-time faculty member at the health science center, is also working on a doctorate in philosophy with a specialty in medical ethics at the University of Dallas. Before he joined the UT faculty, the physician was a co-chief resident at Children's under Eichenwald. His medical school training was at the University of Colorado, Denver, where Kempe of "battered-child syndrome" fame was chairman of pediatrics. "It was there that I became interested in problems of abuse and neglect," says Heyne. "Of course, his influence pervades the school."

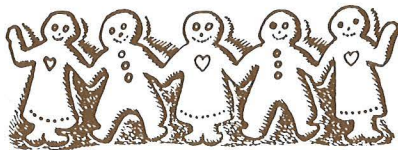
Heyne says that joint programs, such as REACH, which brings together the center, its major teaching hospitals and MHMR, are a part of a national trend in metropolitan areas. Most such programs are begun by or formed in cooperation with medical schools.

The doctor sees some babies and children who are referred by child welfare, some who are sent to nutrition clinic at Children's and still others who come to the attention of physicians in other specialty areas in Parkland Memorial Hospital, the county hospital. All are known or suspected cases of abuse or neglect. Many children are also referred to him through the emergency room.

If maltreatment is part of a medical diagnosis, it is often important to see that the child is brought back for further care, so there is a close coordination with the county welfare department. Sometimes there are other children in the home who need help, too. Psychological or developmental skills testing may be indicated. Therapy, sometimes for the whole family, may be a need.

"Not only are we trying to better the quality of life for whole families," Heyne says, "we are literally trying to save some of these children's lives." ■

Ann Harrell



Probing the plight of the Pimas

Ancient tribe's 'thrifty genes' may hold clues to metabolic mystery

By Chris Land

Photography by Susan Wilson

For more than 2,000 years, the Pima Indians have lived in a remote river valley in the Arizona desert. Genetically isolated, they survived by adapting to cycles of feast and famine. Now, however, the "River People" have fallen prey to the twin maladies of diabetes and obesity.

With the highest rate of diabetes ever recorded, the Pimas are receiving special attention from some of the world's top scientists in an unprecedented effort which may reap benefits for everyone.

Fifty percent of the Pimas aged 35 years and older are diabetic — 15 times the overall U.S. rate — and almost all adult Pimas are obese. Because of this extraordinarily high incidence of diabetes and obesity, the Pima Indians are an ideal popula-

tion for study of these important related diseases, notes Dr. Roger Unger, professor of medicine at The University of Texas Southwestern Medical School and senior medical investigator at the Dallas Veterans Administration Hospital. As a result, the National Institute of Arthritis, Metabolism and Digestive Diseases (NIAMDD) is currently funding a research unit for the study of human diabetes in Phoenix with UT Southwestern Medical School as the contracting institution and Unger, an internationally recognized diabetes researcher, as the principal investigator. NIAMDD is one of the National Institutes of Health.

Diabetes, a metabolic disease characterized by high blood sugar, and obesity have increased in the

United States during the last 30 years, and Indian tribes in the Southwest have been especially hard hit. The creation of a research unit in this area, capable of attracting the world's top experts on diabetes and related disorders for interdisciplinary conferences and collaborative projects, is the goal of this major effort. So far, scientists at 16 different institutions have agreed to collaborate, including: the University of Geneva, Switzerland; the University of Chicago; the University of California at San Diego; Harvard University; the Salk Institute in California; and the Bronx, N.Y., VA Hospital. The group of scientists includes two recent Nobel prize winners.

"This effort may be unique in medi-



cal history because we are assembling from all over the world the scientific talent required to explore a problem in a single population," Unger says. "The research program now has at its disposal the most distinguished panel of collaborators that can be assembled for such a collective research effort."

The first two years of the contract have proven the feasibility of the project, he continues. "Indeed, this may be a preferred method for the solution of certain types of medical problems."

The diabetes unit is located in the Phoenix Clinical Research Center, an NIAMDD-supported facility directed by Dr. Peter Bennett. Bennett is a preeminent epidemiologist who has studied the Pimas for over a decade. Unger says Bennett has produced "the most comprehensive epidemiological data ever compiled on diabetes in a population."

Writing about his studies in a recent issue of *Diabetes Forecast*, Bennett said: "While we still do not know the basic reason why so many of the Pimas develop diabetes, it is unequivocally clear that there is an inherited predisposition to the disease. Following whole families over



Dr. Roger Unger, principal investigator for the NIAMDD study.

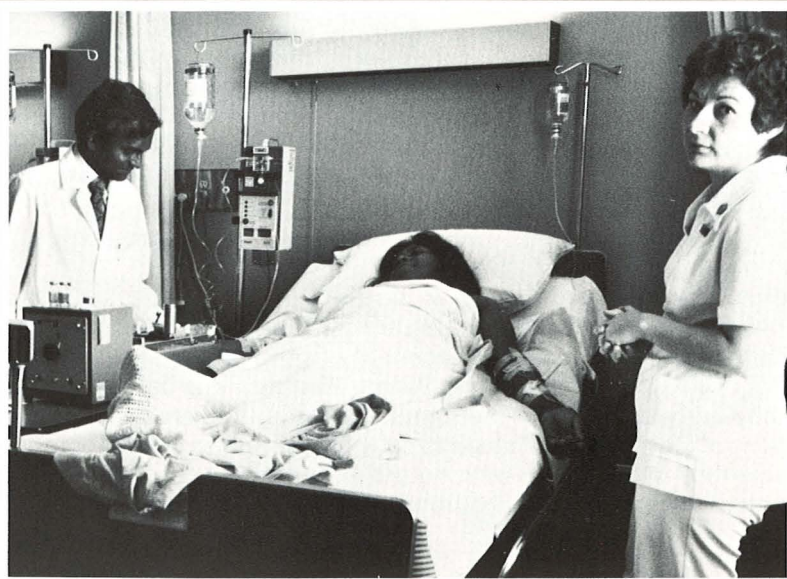
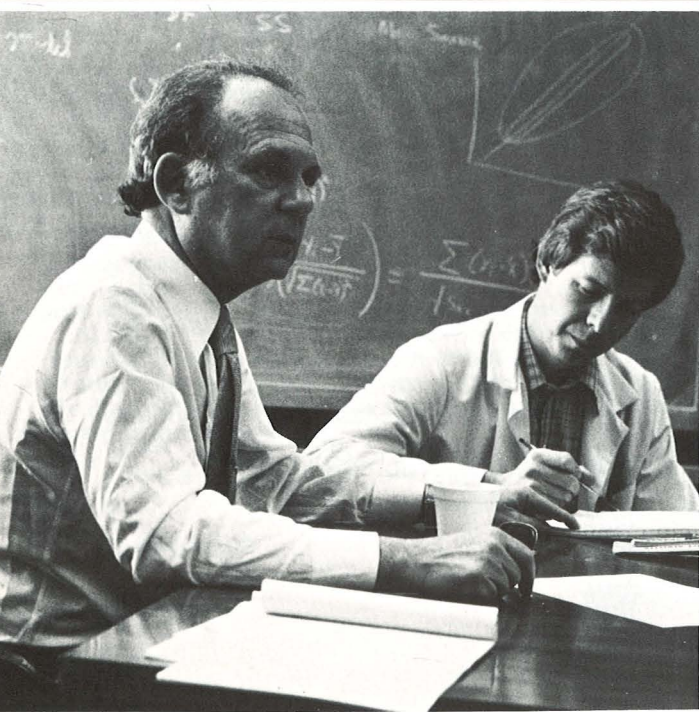
a long period of time will ultimately enable us to determine what proportion of the children of various types of parents — two diabetic parents or a diabetic mother and a non-diabetic father, for example — will subsequently develop the disease. In this way, just how diabetes is inherited will become apparent."

Unger adds that this epidemio-

logical data will be invaluable to researchers conducting other types of studies — studies that would not be possible otherwise. For example, Bennett also can predict which young Pimas will be obese in adulthood. This could be vitally important to researchers because after a person becomes obese, it is difficult to sort out cause from effect. In other words, many of the abnormalities seen in such a person may not be the cause of the obesity, they may just be a result.

An important reason for concentrating research efforts on the Pimas is that they are a genetically homogeneous population. Archaeological evidence indicates the tribe has lived in the same river valley for more than 2,000 years. In fact, they call themselves the "River People," and several centuries before the time of Christ their ancestors were irrigating fields of corn by means of a remarkably well-engineered canal system. Since that time most Pimas have married within the tribe. Also, most eat basically the same diet and have the same lifestyle. So they are a homogeneous population in terms of the two key factors thought to be involved in development of diabetes

Continued on p. 14



Above: Dr. Nagulesparun checks the progress of tests being run on a research volunteer.

Left: Though based in Dallas, Unger makes several trips a month to the Phoenix Clinical Research Center.

Diabetes and drought plague 'River People'

Some 40 miles south of Phoenix, in a dusty river basin crisscrossed by empty irrigation canals, sprawls the Gila River Indian Reservation, home of the legendary "River People" — the Pimas of Arizona.

The Gila River once fed precious moisture to this agricultural people. But upriver dams built nearly a century ago hold back the water, and the once-fertile fields and wooded valley have been reclaimed by the desert. Only barrel cactus and a few tamarack trees spot the barren landscape.

For more than a decade, efforts have been under way to combat the economic plight of the struggling Pima tribe, by restoring irrigated agriculture and developing light industry. But economic hardship is only half the difficulty facing many of the ancient Pimas.

Tribal members Carl and Mary Lewis (not their real names) and at least two of their five children are diabetics — as are more than 50 percent of the tribe. Like almost all the Pimas, they are well aware of the ramifications of the disease, and the intensive scientific effort under way on their behalf. They and their children over

age five are members of a pool of more than 6,000 residents of the reservation who report every two years to the clinic for extensive testing.

They come into the clinic for systematic examination at the specially built NIH clinic adjacent to the Sacaton Public Health Service Indian Hospital located on the reservation. They will be given glucose tolerance tests, electrocardiograms, X-rays, blood tests, a complete physical examination and blood-pressure measurement. Photographs of the inside of the eye will be taken to look for evidence of diabetic retinopathy. And when they leave the clinic, the work will be just beginning. Test results and workups will be sent to the Phoenix Clinical Research Center, where all findings are entered into a computer master file for further research.

While diabetes is a fact of life for the Lewis family, their lives are often governed by the more pressing need of surviving day to day. Tonight they've gathered around the table in the tiny living area of their home to eat a meal of fried bread, beans and potatoes. Not the best diet for a diabetic family,

but cheap and filling. For a special treat, they are having chocolate cake in honor of their son Paul's birthday. Paul, 19 today, is one of their diabetic children.

"You caught us," laughs Mary. "We're diabetics," she says, pointing to her husband and son, "and we're eating chocolate cake." Mary is well aware of the ravages of diabetes. Her youngest child spent the first year of his life in a hospital due to complications she experienced during her pregnancy — complications brought on by diabetes.

"Joseph has hypoglycemia," adds Carl, gesturing to his young, heavy-set son. "The doctors say he will be a diabetic before the age of 30." Behind Carl on the couch, his one-year-old granddaughter bounces and coos, held safe in her mother's arms. More than likely, little Della will begin the biennial visits to the clinic when she becomes five. And statistically, the chances are more than 50 percent that Della will be a diabetic by the time she reaches adulthood — unless the research being done today changes the destiny of the Pima children. ■

Susan Wilson



Above: The Pima Indians of the Gila River Indian Reservation live their lives surrounded by the stark beauty of this semi-arid region of Arizona — a once fertile and wooded valley, now reclaimed by the desert.

—Photograph by Darryl Baird



Top: fried, or pan, bread is a staple of the Pima's diet — a diet that poses a serious problem for a people suffering the double threat of obesity and diabetes. Center: an abandoned wheelchair makes a great gathering place for these Pima children. Bottom: Cyrus and Eleanor Johnson are diabetics who participate in the screening program at the reservation.

— Photographs by Susan Wilson

Probing the plight of the Pimas

Continued from p. 10

and obesity: heredity and diet.

Of course, this is not the case in the general American population, which is a "melting pot" full of people of Oriental, African, and Northern and Southern European origins, among others. And Americans in general have a wide range of diets and lifestyles, which again makes it difficult to get any reliable scientific data. "There are so many different factors involved when you study the general population that it becomes very hard to interpret your data," Unger explains.

Further complicating such studies is the fact that diabetes is not one but several different diseases with similar symptoms. The chance of finding one defect, or one group of defects,

that cause or contribute to diabetes and obesity is much greater in a homogeneous population such as the Pima. "I think it's clear that you can only get so far if you just study the people who happen to live around your medical center," Unger says. "You really need special populations to study certain problems."

The majority of diabetic Pimas develop the disease as adults. Thus, they are said to have "adult-onset" diabetes. About 90 percent of U.S. diabetics suffer from this form of the disease, so results from the Pima studies should be applicable to a large majority of all diabetics.

When diabetics of the adult-onset variety gain weight, their diabetes often gets worse; when they lose weight, their condition improves.

Sometimes all evidence of diabetes vanishes in those with milder forms of the disease if their weight is corrected. Obesity clearly is one of the risk factors for adult-onset diabetes. But, of course, there are plenty of obese people who are not diabetic. Genetic risk factors are also involved.

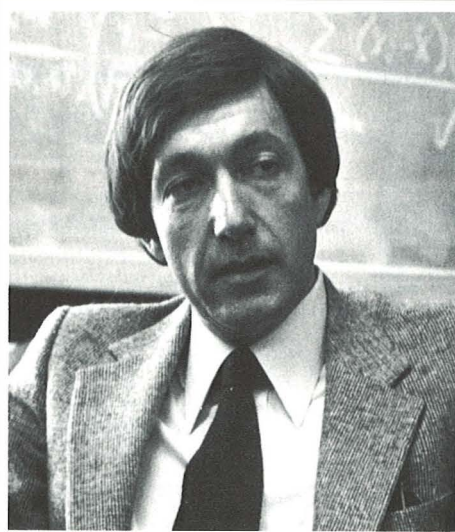
Although the Pimas usually don't become diabetic until adulthood, many of them do become obese in adolescence. Unger believes this is a growing problem in the general U.S. population too:

"I think there has been an increase of obesity in the young here in the United States to the point that it has become a terribly serious problem. I'm not talking about the middle-aged person who gets a little heavy around the waist. I'm talking about people under 35 who are massively obese. I believe this is a relatively recent phenomenon. And when this generation reaches middle age, they may be susceptible to a number of serious health problems including diabetes.

"Obesity on the scale that it exists in the United States is pretty unique," he continues. "It's not really seen in any other country, at least not to this degree. I think it's a shock to people coming from overseas when they see how much obesity there is in this country."

The ability to get fat was of survival value to the Pimas back when their crops were failing an average of once every five years because of drought. Those who became fat during times of plenty had a better chance of living through periods of famine.

The desert rat has made a similar adjustment to life in the arid Southwest. When it rains and there is a lot of food available, the desert rat eats



Left: Dr. Philip Raskin, a Dallas-based member of the team, works closely with Unger on diabetes research.

Right: George Addy of NIAMDD coordinates work done at the reservation clinic and at the Phoenix center.

and eats and gets very fat. When the dry season comes, he has stored enough fat to survive till the next rainy season. But if you put the desert rat in a cage and give him plenty of food year round, he "gets so fat he can barely move," Unger says.

Researchers have theorized that this may be analogous to what is happening to the Pimas and some other Americans who have what one scientist labeled "thrifty genes," that is, genetic factors that in the past would have enabled them to survive when food was scarce, but now are contributing to their obesity because food is plentiful.

In this analogy the "cage" is the American lifestyle and diet, where food is always available. The situation is especially harmful to young Americans. "From an early age these kids are surrounded with easily available food," notes Unger. "In the past people had to go to a lot of trouble to get food, but now there are vending machines everywhere and fast-food places surround the campuses of most high schools and colleges."

Those who don't have the genetic capacity to get fat will stay relatively thin even when they overeat. This has been tested by a group at the University of Vermont now collaborating in the Pima study. The Vermont researchers fed lean prisoners a very high-calorie diet — about three times their normal intake. The prisoners gained only about 15 pounds and then their weight leveled off. In order to maintain the extra weight, the prisoners had to stay on a high-calorie diet. In contrast, an obese Pima can maintain a weight of 300 to 400 pounds on a relatively small number of calories per day.

Some of the Pimas have been able to lose up to 100 pounds by spending several months in the Phoenix Clinical Research Center where their diet can be rigidly controlled. In these patients the investigators are studying differences in fat and sugar metabolism before and after the weight loss, trying to determine why weight loss results in such marked

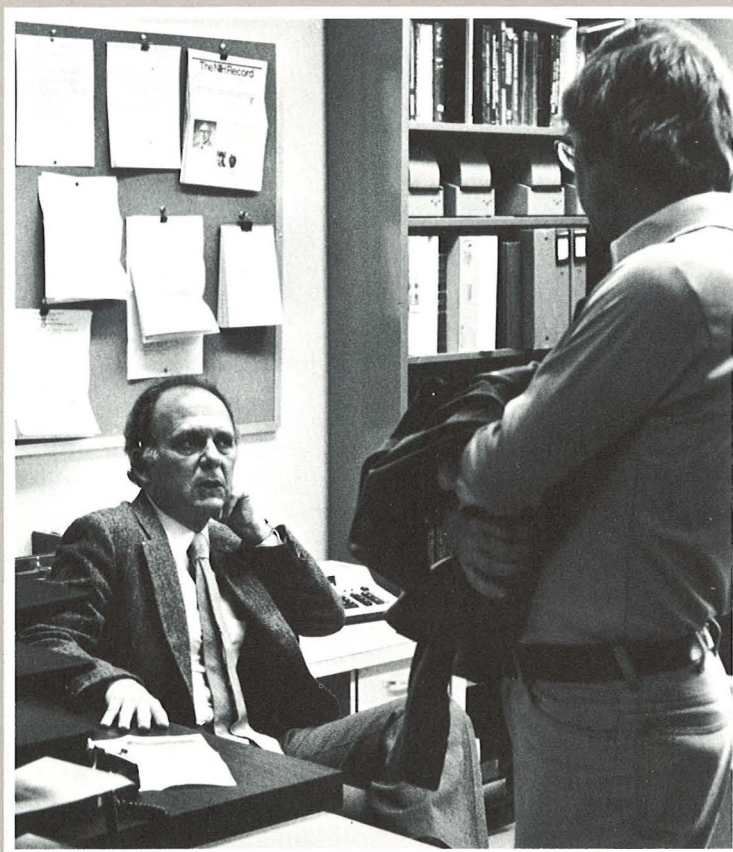
improvement in diabetics.

The various participating research groups are also conducting further studies of glucagon and somatostatin, two hormones known to be involved in the syndrome of diabetes and obesity. Unger has produced evidence that both hormones play important roles in the regulation of blood sugar levels and may be useful in treating diabetes. In addition, preliminary studies indicate that somatostatin may have the ability to slow down the absorption of sugars and fats in the gastrointestinal tract and in this manner it may play a key role in obesity. "It's possible that abnormalities in somatostatin may be present in both diabetes and obesity"

Unger says.

Much of the work on these and the other studies going on at the Phoenix research unit is performed by an "on-site" staff of medical scientists, which includes Drs. Murugasu Nagulesparan, Barbara Howard, David Mott and Frank Kosmakos. Together with scientists at the 16 participating institutions, this outstanding team of researchers is following leads that may result in improved treatment and prevention of diabetes and obesity.

Eventually, the genetics and lifestyle of this small, isolated tribe in the Arizona desert may provide a key to survival for the world's diabetic population. ■



Unger talks with a member of the "on-site" staff.

Disability dramatics: a 'trying' experience



Photography by Darryl Baird

Consider a simple trip to a restaurant.

The hostess shows you to a dark corner in the back — you just happen to have a horrible facial scar.

Or the waiter asks your companion what you want to eat — you just happen to be deaf.

Of course, if you're in a wheelchair, you might not have made it through the front door.

"Often society's response to disability is more handicapping than the disability itself," says Dr. Sean Connolly, assistant professor of rehabilitation science at The University of Texas Health Science Center at Dallas. And William Flynn, coordinator of the continuing education program in rehabilitation, agrees. "Even professionals in rehabilitation are not immune to the dangers of preconceived stereotypes of people with disabilities."

To raise awareness of both abilities and disabilities, Flynn and Connolly direct an exercise in simulation of disability for professional counselors and for undergraduate students at the center's School of Allied Health Sciences.

They offer their students a variety of choices — getting around on crutches or in a wheelchair, wearing ear plugs to help stimulate deafness or eye bandages for blindness, or even professional makeup to simulate facial disfigurement. After choosing and donning their "costumes," students go in teams to a public place, such as a shopping center, where for six to eight hours they assume their chosen handicaps. They note their feelings and other people's reactions as well as their physical difficulties.

Connolly recalls he was sold on simulation as a learning experience when he was a graduate student at the University of Arizona in 1973: his task was to go to the Federal Building in downtown Tucson in a wheelchair.

"The building was completely inaccessible. I had to experience going to every door and finding out there was no way for me to get in. There were steps up or down to every door. Even the loading ramp was too steep for a wheelchair. I just had to leave."

Jeanette Johnson, a junior student

in rehabilitation science, also chose a wheelchair simulation. Her reason: "I was terrified of people in wheelchairs." After a day in a wheelchair in her house and at Red Bird Shopping Mall, her terror was transformed into empathy.

"The worst part was at home," she reported. "It took me an hour and a half to prepare a simple lunch — that was with lots of frustration and resting between maneuvers from refrigerator to stove. The kitchen sink was too high, I couldn't get into the bathroom — if I were suddenly confined to a wheelchair, I would have to rebuild my house."

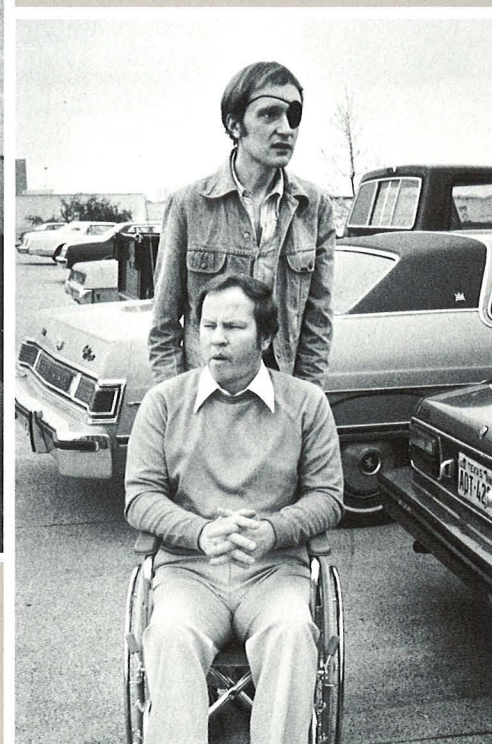
Her situation brought a dramatic difference in reactions at the shopping center. Since she couldn't find anyone to go with her, she pushed her empty wheelchair into the mall. Almost everyone smiled and spoke. "I was doing something nice," she said.

At one department store she pushed the chair onto the elevator, where she was alone, and between floors sat down in the chair. When she wheeled herself off the elevator on the second floor, "suddenly no-



Opposite: Donn Vorse, a Texas Rehabilitation Commission counselor from Houston, assumes the role of a person with a handicap.

Above: Bill Flynn introduces a group of rehabilitation counselors to wheel chair safety. **Right:** Vorse and Harvey Bailey, a TRC counselor from Pampa, Texas, approach a shopping center for their experience as “disabled” persons.



body would look at me.”

Both Flynn and Connolly stress that the handicap simulation is not just an isolated experience. Without work on their feelings, students like Johnson could get stuck in an attitude of pity for the person with a disability.

“This can be a scary, overpowering experience. They have to realize their experience is similar to the *acute* stage of disability. People with real disabilities go through a long process of adjustment, and most develop the ability to cope,” said Flynn.

“There’s no way to get into the mind of a person with a disability. You have this experience that gives you an appreciation of their problems — but you don’t really *know* what it’s like. This, of course, is one of the limitations of simulation as a learning tool.”

Flynn himself often simulates deafness since much of his professional experience has been with deaf people. “This is really hard to do — it’s hard not to react to voices out of my visual field.”

One reason students may find

simulations difficult is guilt — their own guilt about fooling the “audience.”

“We talk about this ahead of time. We just have to look at the higher good: ‘I need this learning experience, and I’m going to be the best actor I can be because if I don’t put this across, I won’t get accurate feedback,’” says Flynn.

Fear, guilt, anger, hostility and embarrassment. All these emotions are discussed in advance, and students are required to write a report about their experiences and feelings and also the feelings they encountered in others. Connolly says this report helps them put their exercise in perspective, and students tell him the act of writing intensifies their experience.

At the first class session after the simulation exercise the stories come tumbling out. The students — undergraduate and professional — can’t wait to share. One who simulated blindness went bar-hopping. She reported that the most empathetic people she met were the cocktail waitresses who invariably guided her hand to her glass so that she

could know where it was. A student in a wheelchair related her embarrassment at trying on shoes. She rolled past four shoe stores before she worked up the nerve to go in.

Connolly sees the simulation as invaluable to his undergraduate students in rehabilitation science as well as all those who plan to work with the disabled. The faculty team presents the simulation exercise also as a key part of the three-week core training program they offer professional rehabilitation counselors.

Once back on the job, counselors report that the simulation was the most important single learning event in the program. Being cast in the role of a disabled person for a short time was a consciousness-raising exercise that helps them relate better to clients with all kinds of problems. ■

Ann Williams

paces

I lost patience with you today
Because our time-frames do not
mesh.

We move in different rhythms
Like big and little wheels;
Like troops on a footbridge,
Breaking stride.

I measure steps in blocks and miles
In runner's luxury of distance.
You march in inches,
In trips from room to room,
Bed to chair,
Chair to porch,
In a cramped odyssey of effort.

Who goes farther?

I with my hare's pace
Touching earth just once in a while,
Rushing past the landmarks,
Crossing the finish line before the
race begins —

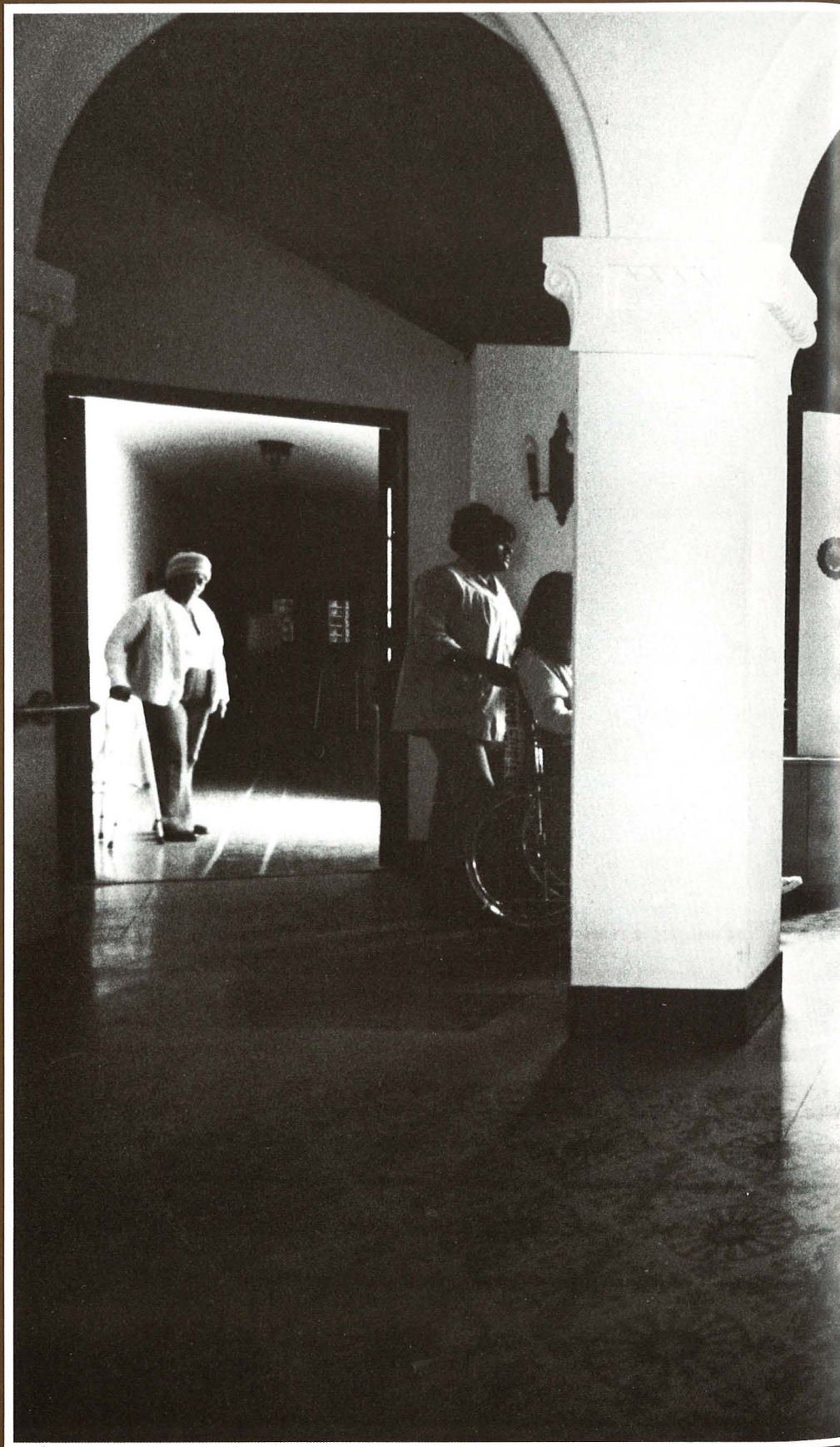
Or you, with tortoise's metered gait,
Dragging slowly,
Sometimes stumbling,
Yet seeing all you pass,
Each step a finish line.

While I teach you to run again —
Teach me to walk.

— Jay Hollon

Medical social worker Jay Hollon was inspired by the people at the Adult Day Activities Center/Oak Cliff of the Visiting Nurse Association of Dallas, where the accompanying photograph was taken.

Photograph by Darryl Baird





Waking up to the power of sleep

By Ann Williams

Photography by Darryl Baird

In 1953 a graduate student in Chicago made an extraordinary discovery. And the "advanced scientific equipment" that made it possible was an army cot, a blanket, a wooden chair, a light bulb painted black on the bottom, a clock, a pad and a pencil. The now well-known discovery was the periods of rapid eye movements (REM) occurring during sleep.

"It really is incredible that until then no one had ever systematically watched another person sleep all night," says Dr. Howard Roffwarg, director of the Sleep Research Center at The University of Texas Health Science Center at Dallas, as he introduces his medical students to sleep research and to the REM stage of sleep.

The Chicago student, Eugene Aserinsky, discovered rapid eye movement (REM) sleep almost by accident. While working under physiologist Dr. Nathaniel Kleitman, he was watching a sleeping friend for eye blinks. Instead of blinks, rapid eye movements back and forth, up and down started about an hour after the volunteer fell asleep. The REMs were exactly like waking eye movements but behind closed lids.

Aserinsky continued the study watching his friend sleep night after night, and found that the REM periods occurred about every 90 minutes during the night. He reported this in *Science* in 1953, but for some reason his report went unnoticed.

In the last paragraph, Aserinsky mentioned, almost incidentally, that when subjects were awakened dur-

ing REM sleep they reported vivid dreams.

Seven years later Roffwarg, a psychiatry resident, heard Dr. William Dement, one of the early stars of REM sleep definition, lecture on dream deprivation. Initially intrigued with the idea of "harvesting" dreams, Roffwarg found his goal quickly changed to studying the relationship between dream images and simultaneous, measurable physiological occurrences.

While working at Montefiore Hos-

***"Sleep that knits up
The ravell'd sleeve of care,
The death of each day's life,
Sore labour's bath,
Balm of hurt minds,
Great nature's second course,
Chief nourisher in life's feast."***
Macbeth

pital in New York City and adding to the meager sleep literature, Roffwarg discovered another physiological phenomenon in REM sleep — middle ear muscle activity (MEMA). This muscle activity occurs in the awake state if a person hears a loud noise or is startled. Now continuing this work at the Dallas health science center with Dr. John Herman, assistant professor of psychiatry, he holds the hypothesis that MEMA during REM sleep is related to loud noises and startle in the dream.

He and others have already found that eye movements coordinate with the imagery of the dream. If someone is watching a tennis game, their eyes

move back and forth from left to right. If the subject is watching a kite ascend, the eyes move up.

They have also found that when the dreamer experiences body movement, electrodes can determine actual muscle activity in the same limbs.

After working on sleep for 18 years, the question that intrigues Roffwarg most, however, is "Why do we need REM sleep?"

There is now no question that we do need it. All mammals do.

REM sleep deprivation studies done on humans in which subjects were awakened whenever they entered the REM state indicate a tendency for REM sleep to intrude more and more frequently. By the fourth or fifth night, 100 to 200 awakenings were needed to keep the subject from having REM sleep. And always on the first night they were allowed to resume uninterrupted sleep, they spent nearly half of their time in REM sleep rather than the usual 20 percent.

Other experiments in interrupted REM sleep over 15 nights left the subjects irritable and uninterested in sex, though very interested in food. Some also had delusions of persecution. When finally allowed to sleep without interruption, they experienced a full "REM-rebound." This showed that "some unknown metabolic processes may be postponed for days before they proceed," said Roffwarg. But eventually the need for equilibrium must be met.

Although still uncertain about REM sleep function, Roffwarg leans

Scientists plumb the depths of slumber for clues to the workings of the mind

toward the hypothesis that REM sleep is necessary for the development of the central nervous system. This would explain his discovery that newborn babies spend 50 percent of their sleep time in the REM sleep stage.

Other evidence of the role of REM sleep in development has been found. The first sharp increases in secretion of luteinizing hormone (a stimulator of estrogen) appear during REM, sleep in girls entering puberty. Also, in fetal sheep the first respiratory movements are seen during REM sleep. So perhaps rapid eye movement sleep is a time when many developmental advances are triggered.

The question then remains, however — why does the adult with a mature nervous system need REM sleep?

This stage may be necessary to produce or metabolize biochemical neurotransmitters and protein for

the brain. Possibly each of the three stages — REM sleep, non-rapid eye movement (NREM) sleep and awake — provides biochemical fuel for the next. Does REM sleep produce norepinephrine (a biochemical related to nerve impulse transmission) or use it? This is not known, but it is probably one or the other.

Another hypothesis is that during fetal development REM sleep particularly primes the drive systems, such as drive for food, necessary for the organism to survive in the environment.

Many questions about sleep are being considered by the research team.

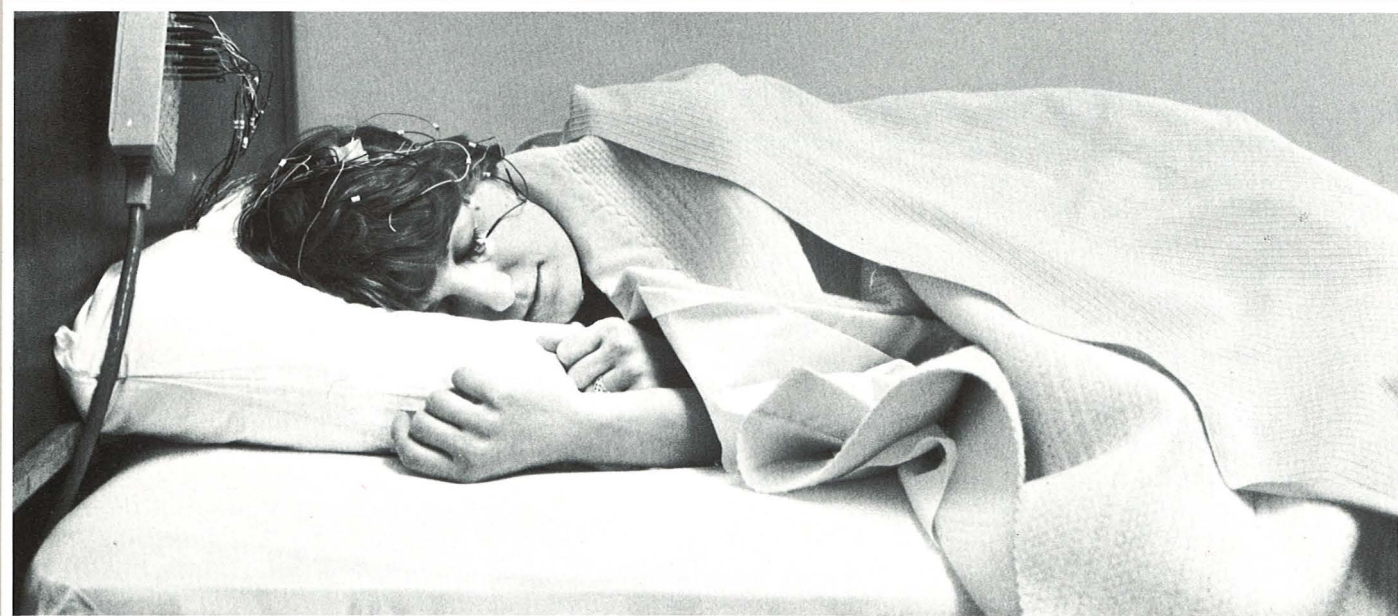
On the nervous system development hypothesis, Roffwarg and Dr. Jorge Farber, assistant professor of psychiatry, plan a study of the effects of REM sleep deprivation in newborn animals.

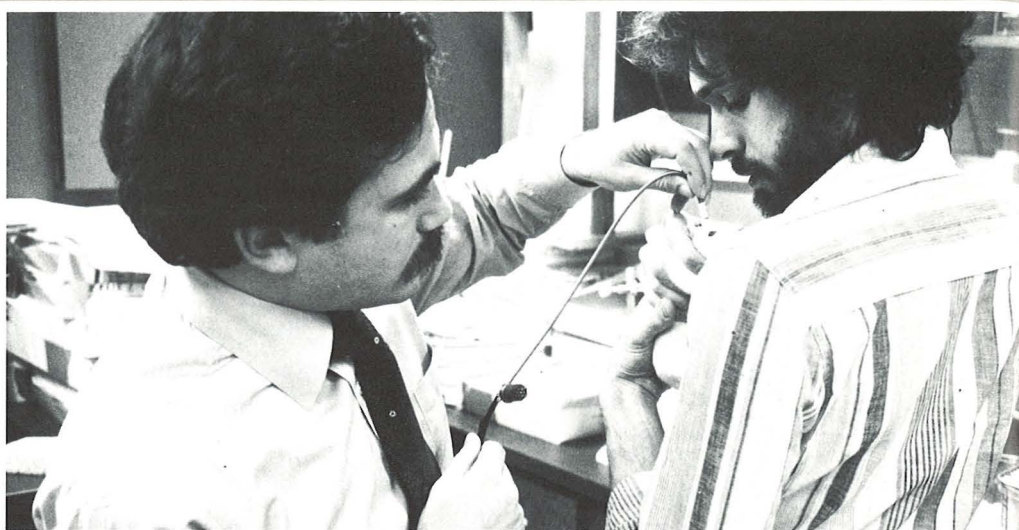
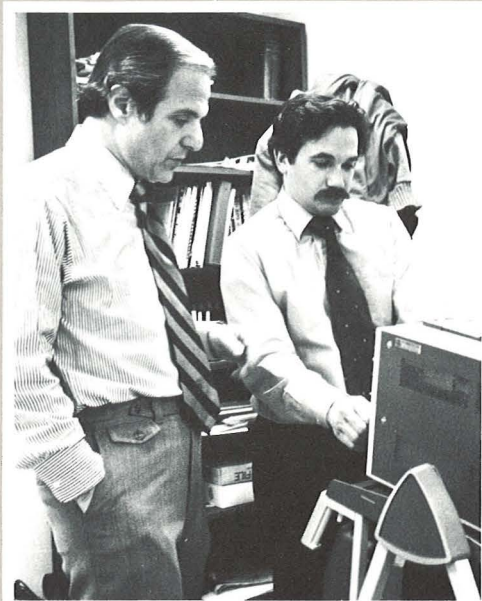
Although it cannot be confirmed that newborn babies and animals

have dreams, they show the same physiological signs during REM sleep that adult humans show in conjunction with dreaming. Babies make sucking motions, rats' noses twitch and dogs growl during REM sleep.

In this state it is as though the organism is awake except for complete muscle atonia (a kind of paralysis). If not for muscle atonia, a fetus would be so frenetically active no mother would be able to endure a full term of pregnancy. The first REM sleep occurs about 90 minutes after an adult falls asleep. The NREM-REM cycle remains about the same length, but the REM periods increase in length toward morning.

During this state the heart rate, respiratory rate and the electroencephalogram (EEG) resemble the active waking state. Men experience penile erections, and women experience increased vaginal blood flow. All this physiological activity takes





Left: Dr. Roffwarg and Dr. Farber study REM sleep in animals. Above: Farber and Mitch Rubinstein measure brain activity of the rat during REM stage.

place along with the eye movements, the middle ear muscle activity and generalized, but damped impulses to the body's muscles. In fact, researcher Michel Jouvet calls REM sleep the "paradoxical sleep" state because of the intense activity going on in the individual apparently at rest.

"Brain-storming," as some call REM sleep, takes on a new meaning as the recesses of the mind are activated into the intense feelings and imagery in the dream. During dreams the stimulation of the central nervous system occurs from within the subject's brain. The same kind of stimulation in the awake state comes from outside the body. Farber and Roffwarg will be trying to find the internal source of excitement to the sensori-motor systems during the dream that, in turn, causes the physiological discharges.

According to Farber, certain areas of the brain regulate and perceive the sensory experience of the dream, and he plans to measure the activity of those areas during REM sleep and to investigate the connections between those brain areas and the nerves of the visual and auditory sensory systems and the nerves that control the eye and middle ear muscles.

This mysterious and intriguing REM sleep, though achieved without

effort, is a complicated process.

"There is a congruity of functions that cause rapid eye movement sleep. Sleep disorders occur if all these functions don't 'meet' at the right time," says Farber.

One such disorder is narcolepsy, in which the patient has sudden "sleep attacks" and persistent sleepiness during waking activity. This neurological problem affects more than 80,000 people in the United States. The premature triggering of the REM sleep mechanism, which causes the "narcoleptic naps" during the day, also causes the patient to go immediately into REM sleep at night without first going into NREM sleep. Following this, the patient awakens frequently, paradoxically suffering from insomnia.

A condition known as sleep apnea is often confused with narcolepsy because of excessive daytime sleepiness. But it can be distinguished from narcolepsy by heavy snoring, the apnea "trademark." Many of these patients are obese and suffer from high blood pressure. These patients literally stop breathing many times during the night's sleep, each time momentarily arousing to the point that breathing is possible. They are unaware of the breathing difficulty at night. Rather they seek help for excessive daytime sleepiness.

Nocturnal myoclonus and the often related "restless legs" syndrome are forms of insomnia in which the twitching of the legs awakens the patient. Roffwarg speculates that this condition, like other sleep disorders, may represent aberrant and uncontained REM state processes.

Sleepwalking and bedwetting are other common sleep disorders, occurring during the deepest stage of NREM sleep. Even "jet lag" involves a disruption of the sleep-wake cycle.

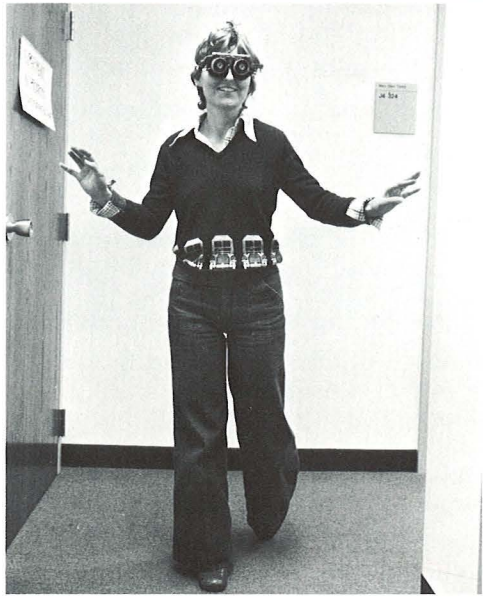
As chairman of the Sleep Disorders Classification Committee of the American Association of Sleep Disorders Centers, Roffwarg is helping to describe the criteria for diagnosing sleep disorders.

While these sleep disturbances are of clinical interest, the sleep team's research will be focused on more basic issues. As Farber works on the REM sleep neurophysiology, determining what is going on chemically and electrically within the brains of animals, Herman will be correlating human physiological measurements in sleep with dream images and awake activities.

The "graveyard shift" in the sleep lab is not all that bad, says Herman. It just means the senior researcher is subject to calls at home between two and five in the morning when the sleep technician awakens a subject for dream recall. Thus, over the



Above: Dr. John Herman establishes an awake eye-movement baseline for each subject. Right: "tunnel vision" goggles limit wearer's field of vision to 30°.



phone, the researcher does a detailed, precise interrogation about dreams.

In the awakenings they try to establish details and "richness in the fabric of the dream." Where were you? Who else was there? What were you doing? For these studies they accept only "good dream recallers."

"This gives us a biased sample, but when you're doing a physiological study of dreams, you need precisely recalled dreams," he says.

In conjunction with understanding the relationship between the physiology and content of dreaming sleep, the Dallas researchers are studying how the awake experience influences dream content.

With a set of "tunnel vision" goggles they're researching the effects on dreams of alteration of awake eye movements. The goggles, constructed with door peephole lenses and worn during all waking hours, limit the wearer's field of vision from 210 degrees to 30 degrees. Therefore, volunteer subjects must spend several days in the sleep lab suite. While it would not be mistaken for the Waldorf Hotel, the suite is quite comfortable with a small kitchen, contemporary prints on the walls and, of course, television. Subjects are encouraged to invite family and friends in to visit so they won't feel isolated.

At night when the subject is ready for bed, electrodes are attached to the scalp for EEG, around the eyes for careful recording of the eye movements and to the upper neck for measuring muscle tone. The electrode cords are several feet long so they don't interfere with the sleeper's movements. The bedroom door is closed and the technician monitors a polygraph recorder two rooms away. The rooms are in constant communication via intercom, there is a phone hookup to the home of the researcher on duty, and all conversation is recorded on tape.

Roffwarg and Herman have pioneered in work on the effects of waking experience on dream content. Most people do not remember color in their dreams. So to see whether color in the waking experience influences dreams, they and others, while at Montefiore, did the "red goggle" experiment.

Subjects wearing red goggles for several days experienced both a reddish tint in the dream scene and an increased frequency of red objects in the dream. This was accompanied by a decreased frequency of blue and green objects. Thus the brain incorporates the current waking experience in dream content, even in the "background." They showed that perceptual change itself (without emotional counterparts) was ca-

pable of altering dream color.

Their current color experiments involve split goggles or split contact lenses with one-half the lens red and the other half blue-green. The right side of the eyes are connected with the right hemisphere of the brain, and the left with the left hemisphere. It may be that if one hemisphere of the brain is more in control than the other, more of its color will show up in the dream. And possibly another piece of the sleep puzzle will fall into place.

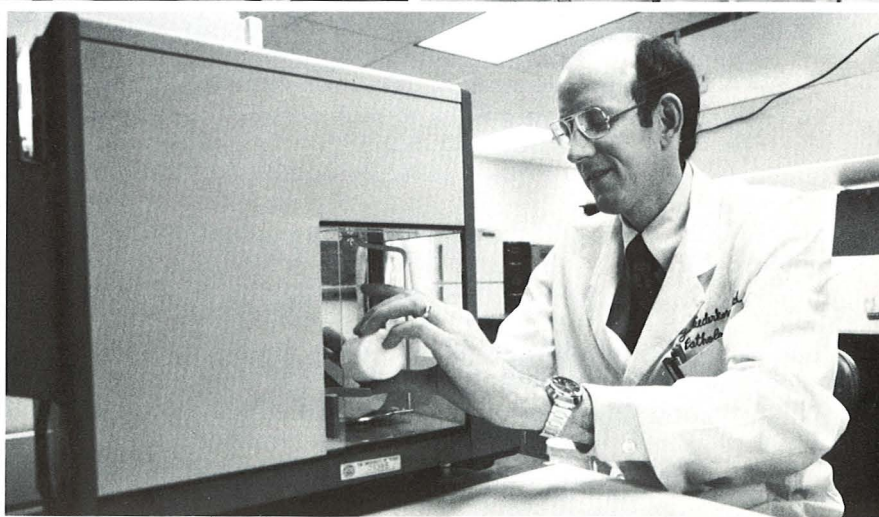
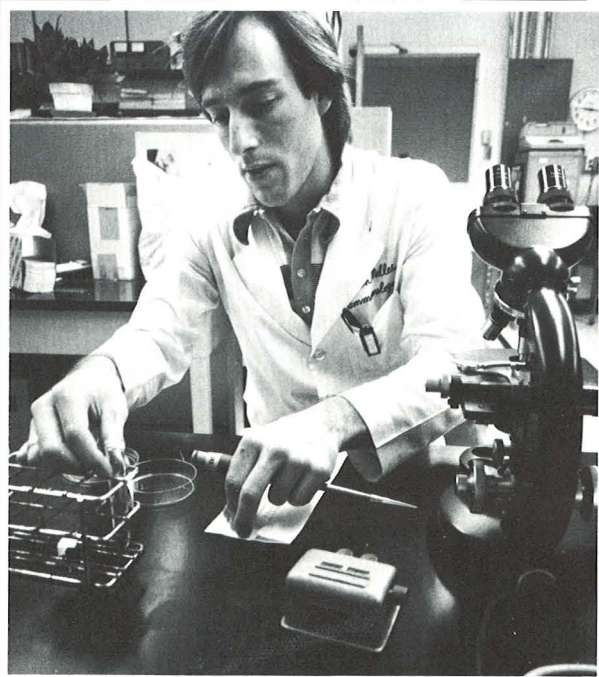
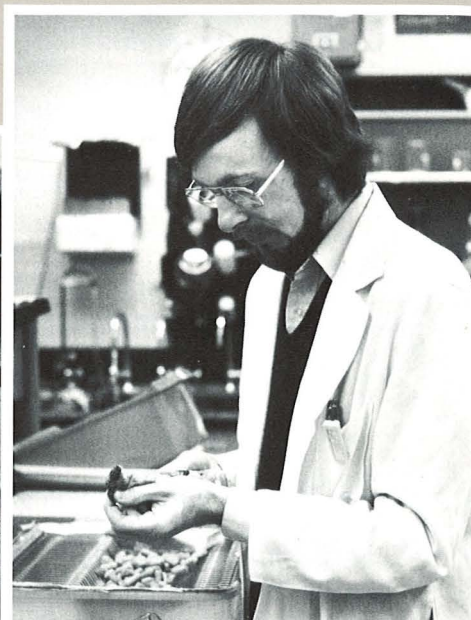
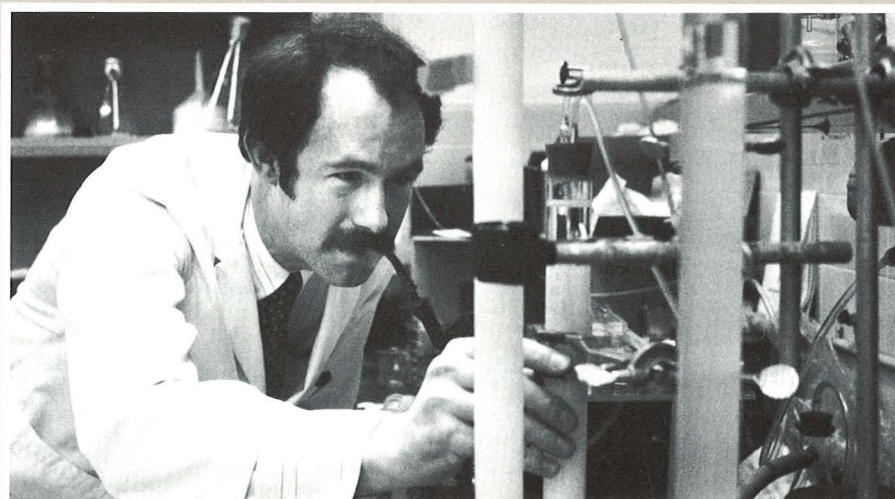
The relatively new sleep center with its up-to-date and specially designed equipment and its staff of 10 conveys the respectability of the 26-year-old science. A far cry from 1953 when Dement could not get electroencephalographers to interpret his REM sleep EEGs because he had slowed the recorder down to one-third speed to save chart paper.

The new science of sleep is fascinating — but is it really important?

Herman answers thoughtfully: "It allows us to understand how the brain and mind work together away from outside influences, and how the mind may create. And the internal generators of the mind are undoubtedly related to every existing mental disorder."

From pad and pencil to microelectrodes in just a few years. And the psychiatrists, psychologists and neurophysiologists may soon be able to tell us exactly how sleep "knits up the ravell'd sleeve of care." ■

Immunology Students not immune to discovery



From upper left, clockwise: Dr. Bill Garner uses gel chromatography to isolate a substance that kills certain mouse tumors. Jeff Farmer injects a mouse to test human plasma for immunosuppressive material. Dr. Jerry Niederkorn weighs out a salt in preparing a medium to grow cancer cells. Mitch Nelles counts living tumor cells from a hamster with the aid of a phase contrast microscope.

Photography by Darryl Baird

“there are still so many questions to be answered.”

Scientific discoveries are not the exclusive province of the professor. Some of the most significant and interesting findings have been made by students. Penicillin, for instance, was discovered by a French medical student in 1896 although his report was ignored.

With the idea that research is an excellent way to teach, the Graduate School of Biomedical Sciences component of The University of Texas Health Science Center at Dallas is involving immunology students in high-level cancer research. Most students have already published scientific papers on their work by the time they finish their training.

In fact, Dr. Wayne Streilein, director of the graduate immunology training program since its inception, says the program attracts some of the best young minds in the country. This is possible because the program receives approximately 100 applications each year from students nationwide to fill six positions. “It’s at least as competitive as getting into medical school,” says Streilein. “Students typically choose our school instead of the best Ivy League and California schools.”

Many of those students are turning their attention toward the relatively new area of cancer immunology.

Working in Streilein’s lab, Mitch Nelles has discovered an unusual antibody molecule on the surface of cancerous plasma cells in hamsters. His finding suggests that it might be possible to control malignant cells with other antibodies specific for these unusual molecules.

Jeff Farmer, a pre-doctoral student, and Dr. William Garner, a post-doctoral fellow, are working on a project with Dr. Morton Prager, a professor of surgery and biochemistry and a tumor immunologist. The team is studying proteins produced by tumors, proteins that seem to

protect the tumor from the body’s immune response. The immune system is one of the body’s primary anti-tumor defense mechanisms.

Post-doctoral student Dr. Jerry Niederkorn’s studies of malignant melanoma in the eyes of cats may eventually lead to improvements in the treatment of human ocular melanoma. Niederkorn works with Dr. John Shaddock, associate professor of pathology.

Molecular events occurring on the surface membranes of cells are crucial in the recognition and destruction of malignant tumors. Graduate student Jerry Fulton has identified enzymes that react with molecules on the surface of certain white blood cells. This model of surface-enzyme modification may reveal key mechanisms responsible for control of malignant cells.

The ability of the immune system to recognize and destroy cancer cells is controlled by certain genes closely linked to genes responsible for transplantation rejection. Several students are studying the molecular structure of the products associated with both sets of genes.

Others have published work on cell surface molecules found in human leukemias, molecules that are important in diagnosis and prognosis.

When the Ph.D. program in immunology began at the Dallas health science center in 1975, it was the first of its kind offered in the United States. This graduate school program was made possible because there already existed a faculty consisting of some of the world’s top immunologists in Southwestern Medical School, another component of the health science center.

By 1970 Dr. Morris Ziff in the Department of Internal Medicine had assembled a strong group of rheumatologists heavily committed

to an immunological approach to rheumatoid arthritis and related diseases.

In 1971 Dr. R.E. Billingham was appointed chairman of the Department of Cell Biology. Billingham and Nobel laureate Peter Medawar had made key discoveries in the area of immunologic “tolerance” in tissue transplantation. One year later, Dr. Jonathan Uhr became chairman of the Department of Microbiology. He had made discoveries about regulation of the immune response that led to methods for preventing “Rh” disease in newborn infants. Thus, the graduate program began in response to this unusual concentration of outstanding immunologists.

At the present, 35 members of the medical school faculty in various departments teach in the graduate school immunology program. First-year students rotate through laboratories learning techniques with three to four faculty members before choosing their specialty areas. “The strength of the program lies in its interdepartmental nature,” says Streilein. “I think this is a successful way for a medical institution with a fixed departmental structure to teach new disciplines that transcend departmental lines.”

Supported by grants from the Department of Health, Education and Welfare, the cancer immunology training program also receives annual assistance from the Ladies’ Auxiliary of the Veterans of Foreign Wars, Texas Chapter. With this aid, students along with faculty are tackling some of the tough questions in cancer immunology. In the words of one student: “I chose immunology because there are still so many questions to be answered. When we find the answers, they will be important to many human diseases, including cancer.” ■

Ann Williams

The Life Connection

Steady strides in transplants and dialysis are reflected in pilgrimage to kidney clinic.

Story and Photography by Susan Wilson

As early as 6:30 every Tuesday morning, they begin to gather in the small, out-of-the-way clinic on the third floor of Parkland Memorial Hospital's bustling Outpatient Clinic. By the official start of clinic at 7:30, there will be as many as 35 kidney transplant outpatients gathered in various examining and waiting rooms — reading, chatting quietly, greeting old friends, making new friends — whittling away at the sometimes anxious hours of waiting. For some of them, this routine is repeated every week; for others, the visit has become a twice-yearly pilgrimage — a morning of blood tests, urine samples, examinations and waiting for the results of kidney function tests.

"The clinic is run sort of loose," explains Carolyn Atkins, who has worked with Parkland's kidney transplant patients since 1969. "The patients get uptight — they want so badly for their kidneys to work. . . Maybe they think their serum creatinine (measurement of renal function) will be up. Or they are afraid something else might be going wrong with their kidney. So the clinic is not a sterile structure."

Operated on a sort of "do-it-yourself" basis, Tuesday morning clinic has become a familiar routine to the patients. Sign in, weigh yourself, pro-

duce your urine sample, have your blood sample taken — run the blood samples down to the lab. By 9:30, examinations begin. With luck, you'll be finished by noon — or you may be there all day.

"If something is wrong with an outpatient's renal function, we have to do all sorts of additional tests and they may be here from 6:30 a.m. to 6:30 p.m." Atkins, coordinator for the Kidney Transplant Clinic, knows most of the patients as individuals. As they become candidates for a transplant, she screens their medical histories, puts their names on a computerized list of patients waiting for a donor kidney and sets up files which will be updated on a regular basis for the rest of the patient's life.

"We see new transplant patients about twice a week," she explains, "then once a month, and finally twice a year. Patients who live out of town get their blood work done and the results are called back here to us. Then, if a patient gets sick, we have up-to-date records. We had a guy call in today with fever and a cough. All the information on him was here when the doctor got here."

At 24, Frank Priolo is one of the "old hands" at the transplant clinic, a component of The University of Texas Health Science Center at Dallas Kidney Transplant Program. He's

taken the morning off from his job as an accountant for Texas Power & Light to undergo the routine tests for a six-month checkup. He won't wait for the final results of his tests. "I just assume everything is going to be okay. If it's not, they'll give me a call anyway."

Frank received a donor kidney from his brother in August, 1973, less than nine months after the onslaught of kidney disease.

"I had never had any kidney problems until my freshman year in college. When I came home at Thanksgiving, I was passing blood in my urine." Frank was diagnosed as having nephritis, a condition involving both kidneys and possibly the result of an ear infection from water skiing that summer. Although he was under constant medical care following his release from the hospital in December, it was obvious by the following March that his kidneys were not recovering.

"There was a definite downward progression and that's when I went on dialysis," he recalls. In anticipation of dialysis, a fistula (a procedure in which artery and vein are joined surgically) had been made in Frank's wrist. "I was really scared that first day on dialysis. Those needles are very large and very scary. The whole experience was hell. I couldn't see



spending my life sitting next to a machine. It's like a long extension cord — you can't go too far without pulling the plug. . . . and sometimes, dialysis can be painful."

For Frank, the decision to have a kidney transplant was easy. "I always foresaw I would have a transplant. I wanted to get everything taken care of, so to speak, and start my life over." Though his surgery went well, he had been warned that there would be an initial onset of rejection. "I had been warned — but I was still depressed when it happened. It is like you know inside it's not working as it should. You know something is wrong and that you might have to start all over again. But I had a good match to

start with, and from the very beginning, I would think about it every night and tell my body it was not going to reject the kidney, that it was my organ."

And Frank's brother's kidney "took," as it does in a high percentage of transplants between siblings with compatible transplantation antigens. Nearly five years later, Frank is a healthy, physically active young man whose only reminder of his bout with kidney disease is his semi-annual checkup at the Kidney Transplant Clinic.

Kidney disease. More than 13 million Americans suffer from some type of kidney and urinary tract disease, according to statistics from

the National Kidney Foundation. And each year, 54,000 die of kidney disease. Another 42,000 Americans suffer from chronic renal disease and need an artificial kidney to stay alive. Fourteen thousand of these victims are waiting for a donated kidney — but only 4,000 of them will receive a kidney transplant this year. Others will wait, sustained by dialysis performed several times each week.

Fifteen years ago, Frank Priolo's chances of surviving the failure of both kidneys would have been minimal. For while the first successful kidney transplant had been performed as early as 1954 between identical twins, there were no other

types of successful transplants in the next decade. By 1961, a regimen of immunosuppressive drugs was developed which held out the hope that the organs of less closely related donors could be successfully grafted — though the drugs themselves could cause intolerable, sometimes fatal, side effects.

The development of the artificial kidney machine was another element vital to the success of kidney transplantation. Already very ill from the effects of body wastes not excreted by their diseased kidney, prospective transplant patients could be brought to a state of reasonably good health through dialysis.

Today, it is possible to maintain a victim of kidney disease on dialysis for years, if necessary, until a suitable kidney becomes available. And dialysis allows them to be maintained if the transplanted kidney fails to function, or is rejected. But in the early '60s, hemodialysis was considered, at best, a stop-gap measure which allowed victims of reversible kidney disease a chance to recover renal function.

In 1964, research at Southwestern Medical School had advanced to the point that kidney transplants could be attempted on humans. Dr. Paul C. Peters, professor and chairman of Urology, had been at the medical school barely a year when the first successful kidney transplant was performed here. The survivor of that historic transplant operation was a 10-year-old girl whose identical twin was the donor. Two other transplant attempts that year failed.

In 1978, 14 years later, 62 kidney transplants were performed here, and the number of deaths had dropped to three. Peters and Dr. Alan Hull, chief of the Kidney Dialysis Unit, have been the guiding force behind the medical school's kidney transplant unit, one of the most successful in the nation. Peters describes the growth and success of the unit in small, painstakingly earned victories.

"Early on," he says, "there were some basic discoveries in immunology that led us to believe that genetic barriers (between two or-

ganisms) might be modified or overcome. Identical twins could be transplanted. And the work of Dr. Billingham showed that the tolerance of tissue from one individual to another was a learned phenomenon, and not genetic." (Dr. Rupert Billingham, a transplantation biologist, is chairman of the Department of Cell Biology at the health science center.) At the same time, new drugs were being developed that might modify an organism's attack on a graft that's not genetically compatible. These immunosuppressive drugs would play a vital role in the success of transplantation.

"Earlier studies suggested to us that transplantation was feasible — that related living donors could be used, and that cadaver donors might also be used on occasion. Although many factors, such as tissue incompatibility, were undesirable, we started out."

Dialysis support was primitive in those days. "But it was obvious from the start that dialysis and transplantation had to go hand in hand. The transplant unit would have

trouble existing without good dialysis support." When perfected, dialysis would allow the stabilization and maintenance of a prospective kidney transplant recipient until a donor kidney could be located.

As mass dialysis became available, large outpatient units were established with the responsibility of actual dialysis transferred to the nurse, technician, or in many cases a friend, member of the family or the patient himself. Mortality rates began to drop as the number of transplants increased. Hand-in-hand with advances in tissue typing and dialysis were improved methods of harvesting and preserving the kidney.

"The ability to keep the kidney in functionally good shape made it possible to ship kidneys all over the world. Development of the computer allowed prospective transplant recipients to be placed on a computer list, and the most suitable recipient for an available kidney could be immediately determined," Peters says. RENTRAN, an on-line computerized kidney transplant matching system, was the outgrowth of a regional



Dr. Alan Hull, a pioneer in mass dialysis for sufferers of kidney failure, talks to six-year dialysis "veteran" Horace Peterson.

registry which listed vital information on potential kidney recipients. Originally conceived by Dr. Peter Stastny, a transplantation biologist at the health science center, the registry was adapted to computer use at the center and is the prototype of a network of similar computerized organ matching systems across the country. "Although some logistical problems still exist, it is now possible to determine suitable recipients any place in the world, once the compatibility factor is known," Peters adds.

Yet despite these advances, the biggest obstacle to overcome remains the body's immunological barrier — its grim determination to reject and destroy any foreign substance that invades it, not only life-threatening microbes but the life-saving transplanted organ as well. New research being done by Stastny, along with an international group of

transplantation biologists, may overcome at least one of those barriers, as they explore a new method of typing for the compatibility of donor organ and host.

If this effort succeeds, the time involved in testing for donor/host compatibility could be reduced from about a week to five hours. This reduction in time would be a major breakthrough when testing for compatibility in cadaver kidneys because these kidneys cannot be preserved for the length of time it presently takes to do the test. This is one reason why cadaver kidney transplants tend to be significantly less successful, with a donor kidney survival rate of about 50 percent at one year.

"To our disappointment, typing for tissue compatibility in cadaver transplants has not proved to be of significant value in determining the outcome of a graft," Peters says. "However, in family groups, these tests play a key role in selecting the best living related donor. Graft survival in recipients of cadaver kidneys has not improved significantly in the past five years in spite of better harvesting techniques and improved preservation."

But patient survival, which stands at about 85 percent in the same one-year period, has improved. Today when failure of the graft becomes evident, it is immediately removed and the patient returned to dialysis to await another, hopefully better kidney match. The recent availability of the drug ATG (anti-thymocyte globulin) has provided a smoother early post-operative course for patients receiving a cadaver transplant. Because it usually delays the initial onset of post-operative rejection, many times the patient leaves the hospital without undergoing an early rejection crisis.

"But rejection does occur eventually, and by the end of two years renal function appears to be about the same in those groups of cadaver kidney recipients whose grafts still survive whether or not they received ATG." At least for the present, Peters sees the major function of ATG as minimizing early rejection, giving the

transplant patient some time free of the dialysis machine.

For the recipient of a kidney from an immediate member of the family — a parent, a child, a brother or sister — the chances of graft survival are much better. Genetically, there is at least a 25 percent chance of identical tissue compatibility between siblings. When this occurs, transplantation between such siblings is successful over 90 percent of the time. And while the graft-survival percentages fall somewhat when the match is not optimum, the rate of survival is still gratifying.

Ask Leslie Oakes.

Oakes was in the middle of a family vacation at Lake Texoma in August of 1972 when he became sick. At 55, he had never had any kidney problems — in fact, he considered himself a healthy person and took care to maintain his good health. But during that weekend, for reasons no one can pinpoint, his kidneys simply stopped functioning. When he returned to Dallas, he was already a very sick man.

"It happened just like that," recalls the robust, gray-haired 62-year-old man. "They put me in the hospital when I got back to town, and I never put out another drop of water until the transplant."

For Oakes, kidney failure was complicated by the fact that he was unable to tolerate dialysis. "I went down from 205 to 138 pounds while I was on dialysis. They would put me on the machine, I would pass out and they would have to take me off. I was going downhill really fast." By November, when it was determined that both his married daughter and his 29-year-old son, Dick, were suitable donors, Oakes had had several cardiac arrests. "I didn't think I could survive to have the transplant."

His son, confined to a wheelchair since the age of two with cerebral palsy, insisted that his dad receive his kidney. "He didn't think his sister should do it with all of her responsibilities, and he really wanted to do this for me."

The transplant was performed in December, 1972, and life for Oakes, retired now and living at Lake Texoma,



Dr. Paul Peters (left), director of the Kidney Transplant Program, discusses a procedure with colleague Dr. Tom Parker during the Tuesday morning clinic.

is "just wonderful."

His health has returned to its pre-kidney failure status. As a bonus, he says his son Dick has been much healthier since he "gave" his dad a kidney.

For 32-year-old Vickey Steinhauser, a strikingly attractive young woman with soft blue eyes and honey-blond hair, a kidney transplant in June, 1972, meant more than just a release from the dialysis machine. Her son, Kyle, born two years after the transplant, is a miracle of sorts. Pregnancy places an added strain on the kidneys, and for a kidney transplant patient, the risks of pregnancy can be inordinately high. But Vickey sailed through the operation, and the kidney her sister gave her never showed a sign of rejection. Her only complication during pregnancy was a slight rise in her blood pressure and a resultant stay in Parkland's high-risk pregnancy unit.

Kyle, now four-and-a-half, accompanies his mom on her trip from Longview for her six-month check-ups, then visits his "friends" in the high-risk unit.

"Our philosophy at the clinic is, 'Once you are transplanted, you are ours,'" explains Carolyn Atkins. "If our transplant patients have any problems, they come to us. If they get a cold or break a leg, they call us first.

We follow them forever. A pregnant transplant patient is followed here, and delivered at Parkland. We take over like the family physician." Currently, the kidney transplant clinic has up-to-date, active records on about 175 transplants, including Priolo, Oakes and Steinhauser.

"It's the only job I know," she added, "where you can follow your patients through to the end. You see them in early renal failure, through dialysis and transplant. If the transplant works, you see them go back to their families, their jobs. If they die — well, they usually die here. It's a full cycle."

Patients of the Kidney Transplant Unit start their life-long association with the unit long before any transplant operation is performed. Victims of long-term, chronic kidney disease or a sudden onslaught of kidney problems that lead to renal failure, most of them will be on dialysis for some time before transplantation.

"We do long-term care planning for every patient that goes on dialysis," Atkins says. "We evaluate the patient as to whether or not he or she is a home-dialysis candidate. And we review each patient's long-term plan yearly."

Not all victims of end-stage renal failure can have or choose to have the surgery. Patients over age 55 fall

into a "gray zone" as possible transplant recipients. (But even age is not a final deterrent — an 86-year-old man recently received a kidney from his 64-year-old son.) Patients who don't have a living related donor may choose long-term dialysis over the risk of failure with a cadaver donor. Despite the continuing growth rate of success in kidney transplants, the survival rate for patients on dialysis, including elderly patients and patients with malignancies, is an astonishing 94 percent at one year. "That's a phenomenal survival rate," Atkins points out.

But some, like Leslie Oakes, just don't do well on dialysis. The ravages of chronic renal disease may make dialysis unacceptable, or they may be emotionally unable to handle the rigors of dialysis. For these patients, a kidney transplant may be the only viable solution. "Some people tolerate dialysis very well — others don't. There is no way to physically tell beforehand what dialysis will do to the body." These patients almost always opt for transplant, and once that decision is made, they become firmly plugged into a life-time association with the Kidney Transplant Clinic.

The decision to ask a family member to donate a kidney is left entirely up to the patient. Then once a family



Above: transplantation biologist Dr. Peter Stastny conceived the idea for the regional registry on potential kidney recipients, a prototype of the national computerized kidney matching system, RENTRAN. Right: Carolyn Atkins, clinic coordinator, and co-worker Mary Lou Guthrie (far right). "Our philosophy is 'Once you are transplanted, you are ours.'"



member agrees to being a possible donor, he or she must contact the transplant clinic. "This is all on the patient and the family's initiative — we want to make sure there is no coercion of a donor," Atkins emphasizes. Tissue typing of prospective living related donors is done to determine the best possible match, the patient is stabilized and surgery is scheduled.

But what of the patient who has no living related donor available?

"When that happens, the patient goes on RENTRAN. Then, as a kidney becomes available, it is tissue-typed for the same antigens. This is the optimum and usually doesn't occur — but we try and find the best possible match."

Kidneys available through RENTRAN are cadaver kidneys, donated either before death through an organ donation program, or at the time of death by members of the family. Peters describes it as literally, "a gift of life."

"It is extremely difficult to ask a father and mother to give up the kidney of their dying child. But for the people involved — for the doctors, and particularly for the recipient — there is undying gratitude that the family is willing to give an organ of the recently deceased."

Fortunately, legislation in this area

is improving. In recent years, there has been an attempt made to define death more precisely to enable earlier removal of organs from cadavers. And more and more, people are encouraged to donate organs through simple forms such as the one included on the back of a driver's license.

For every kidney that becomes available, there are as many as 90 dialysis patients in the immediate area who may be potential recipients. Who decides what person in that group will finally get that kidney?

"People always ask how you decide what patient gets a kidney first. Really, there is no easy answer," Atkins reflects. "The patients usually sort themselves out. We have a list of at least five potential recipients for any given kidney and start calling. Somehow, the patient usually seems to get the call in the middle of the night. I don't know why. Some on the list get frightened at the prospect and turn the kidney down. Or they just got over a cold and are on antibiotics."

"And we do have a priority list that includes the one percent or so who fail to thrive on dialysis. These are people who are doing poorly on dialysis, many losing their ability to be dialyzed. They are the type of people who get priority. They are told, 'If you want the kidney, you go to the hospital right now.'"

Since the RENTRAN system covers a large section of Texas, patients from as far away as El Paso, Lubbock, Amarillo or Odessa may be contacted to come to Parkland for the transplant. Time becomes of the essence, for the "older" a kidney gets, the less are its chances of functioning properly.

"The patient doesn't have much time to think about it," she adds. But the patients have been well prepared beforehand, including psychological evaluation and counseling.

"The patients aren't lied to. We tell them the risks — including the per-

centages of success for living related and cadaver donor transplants. A transplant is no panacea. It's not going to make them beautiful; in fact, just the opposite. Their faces puff up from the steroids. And one of three things will happen: they'll go home with a working kidney — or they'll have a bad rejection, lose the kidney and go back on dialysis — or die from a bad infection."

But once the decision for transplant is made, no time is lost. They go immediately to the transplant unit, where they are prepped and ready for surgery within three hours. A final cross-match is done just prior to surgery to ensure a good match of donor organ and recipient.

And if all goes well, the patient will soon begin the Tuesday morning pilgrimage. ■



Elated at the results of her kidney function tests, this outpatient lets out a happy "all right!" as technician Gary Sumner finishes his computations.

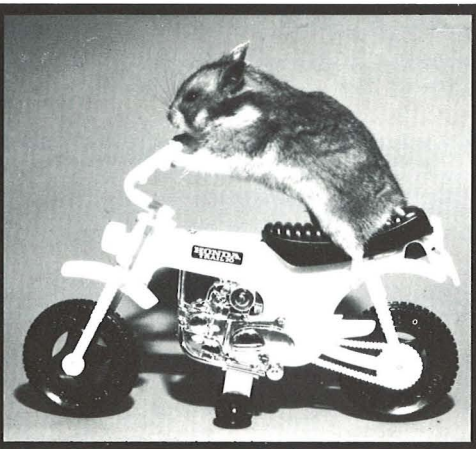
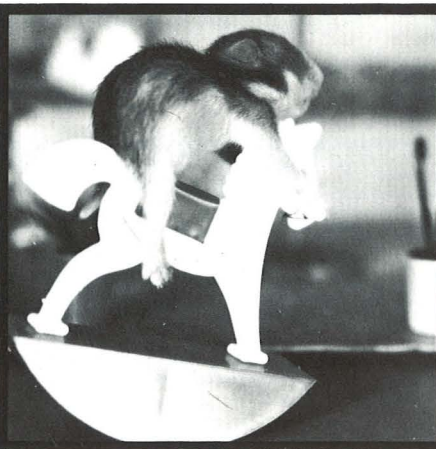
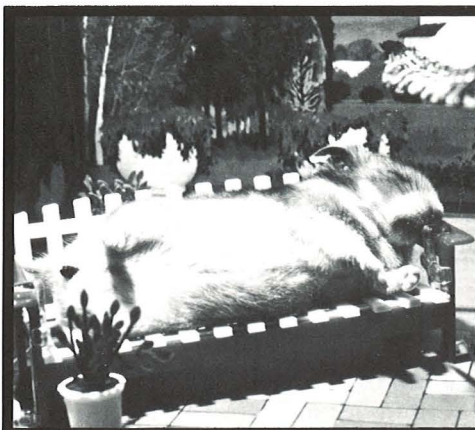
Clark Humble:

An Immunolegend for Our Time

By J. Wayne Streilein

Once upon a time, but not so very long ago, there lived in the enchanted kingdom of Rodentia an affluent, middle class family of hamsters by the name of Humble. Born into this fortunate family was a son of considerable promise named Clark.

Clark enjoyed the good life: his favorite hobbyhorse of younger days was soon replaced by a more rapid means of travel. He buzzed



around Rodentia with abandon: many days found him lolling away his time on a comfortable bench; many other days he sat sunning himself along the Rodent beaches. But as the magic of his youth began to fade, he looked into the mirror one day and

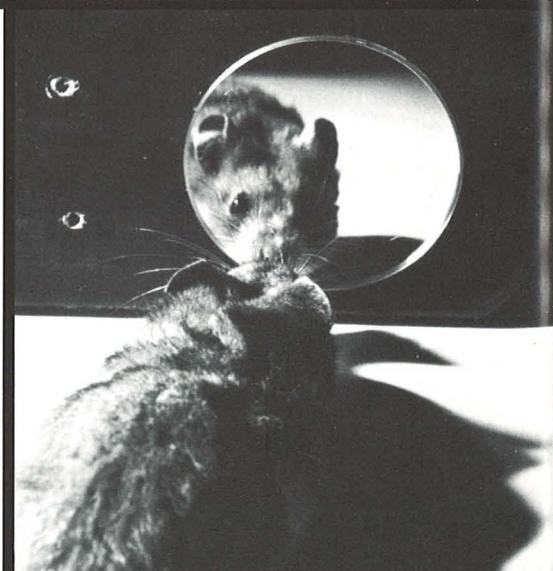
asked himself what the meaning of his life might be. After considerable thought and consultation with his beloved but decadent parents, he realized he could not follow in their bourgeoisie footsteps, nor could he aspire to the prosaic goals they had set for him. Rejecting potentially lucrative occupations in high finance, corporate law, and/or pharmaceuticals, he decided that he must make a

Note: Dr. J. Wayne Streilein is director of the Graduate Program in Immunology at the health science center. His fable was presented with color slides as a Faculty Seminar. A slightly different version appeared in "Immunogenetics" 4:1-6 (1977).

Photographs by James B. Wiesner

contribution to his world — not surprisingly, he opted for a career in science.

Clark Humble journeyed to the regional health science center at Kent where he examined the research laboratories, which he would share with others who had also committed their lives to science. He was at once struck by the validity of his decision for a career in scientific research; he then attempted to discern what contribution he might make, one that would be unique and important. One day he found himself amid a gathering of similarly employed subjects, specializing in the



study of Immunology.

During the conversation that followed, he discovered that Reginald Rattus was especially proud of his contribution to the study of immune protection of tumors: his father, after all, was a pioneer in the experiments which showed that enhancing antibodies could protect a foreign kid-



ney graft from rejection. While more modest in tone, Genevieve Guinea Pig proudly related her remarkable success in displaying positive TB skin tests. But more impressively, he was told — by none other than Gus Musculus himself — that mice had been responsible for most major advances in immunology: the role of the thymus gland in development, the interactions of different lymphocytes, and the genes governing transplantation rejection. Clark was indeed overwhelmed. He quickly realized that wherever he went in research he would find himself increasingly surrounded by mice and by what he called the “Murine Hegemony.”

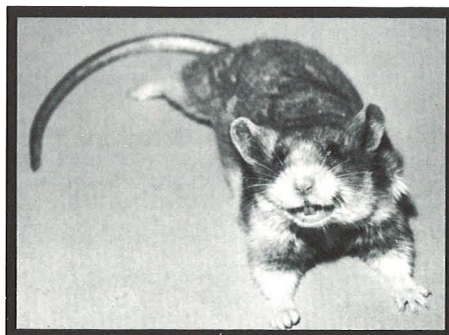
His first few jobs ended in failure: it was found that he was unable to make antibodies to soluble antigens; more disastrously, it was then discovered that he was unable to reject a foreign tumor graft. Clark was finally driven to a very unpalatable conclusion: if he were ever to have a successful career in science, and especially in immunology, he would have to pattern himself after Gus and his kind. He studied mice assiduous-



ly: their habits, their mannerisms, their fetishes and their tails. This last became a symbol of murine dominance.

From the dawn of hamster time, the Humble lineage was blessed with only a rudimentary posterior appendage. Clark became obsessed with the idea of acquiring a sizable tail of his own. Days and weeks passed. All of his waking efforts were directed towards developing a tail to rival Gus. . . .

And then suddenly, one day, just after he had been unmercifully taunted by Gus, “Clark can’t, Clark can’t!” he awoke to discover that he had miraculously grown a posterior ap-



pendage. He had a tail!

He had a tail!

He was ecstatic; his career in science seemed assured. He immediately set out to undertake a prominent role in the advancing front of contemporary immunology.

Within a comparatively short period of time, Clark Humble became avidly sought after for a wide variety of important experimental studies. He proved to be unusually susceptible to many laboratory virus infections and as such was prized by virologists around the world. The ease with which tumors could be induced by tumor-causing viruses or chemical carcinogens made him extremely attractive to tumor biologists. And transplanters were especially fond of his readily accessible cheek pouch where foreign tissue grafts survive indefinitely, to say nothing of the fact that he could reject foreign skin grafts without the help of antibodies.

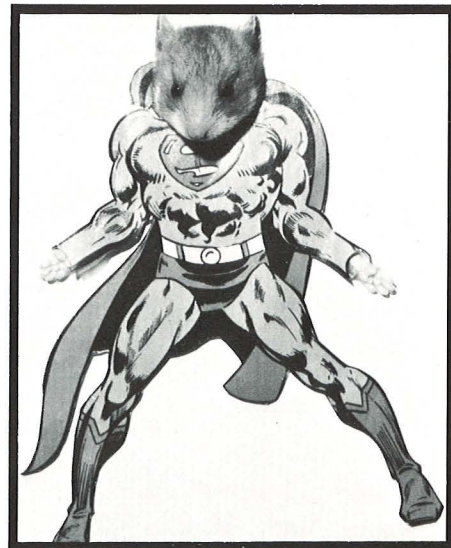
Thus, although he began his career by trying to mimic his murine competitors, he found his true role to be

that of an iconoclast, placed in the midst of the murine-human orthodoxy. Whereas he had initially viewed the world of immunology from the vantage point of a miniscule creature trying to make a place among the throngs of imperious mice, he has come to feel comfortable with these same creatures on an equal footing, although secretly he knows that eventually the dogma will collapse, and he shall be vindicated and dominant.

Surely, his career in science which began as a lowly participant in the Health Science Center at Kent has matured. His remarkable tenacity, his devotion and his realization of his own unique worth gradually paid off, and he acquired a reputation commensurate with his xenocompatriots in immunologic research.

Now, on very infrequent occasions, he returns to visit his native Rodentia. At these times friends and family gather round, and he recounts the marvelous tales of the ultimate ascendancy of hamsters in immunology, not failing to interject that the tyranny of the mouse is destined to end. Then amid heartfelt expressions of admiration, the massed throng of happy hamsters takes up a chant, initiated by one or another hamster pup with personal visions of grandeur, but expressing the aspirations and affection of all:

Clark of Kent!



FRONT and CENTER

Cancer imaging

Two Dallas psychologists believe that patients "in touch" with their illness can help themselves as well as their physicians. Drs. Jeanne Achterberg and G. Frank Lawlis work with "imaging," or imagining the disease process and treatment procedure, to open up communication between the doctor and patient.

The husband-and-wife team recently published "Imagery of Cancer," a book for professionals, which summarizes their research with 90 cancer patients who put pen to paper to draw what they imagined was happening within their bodies' immunological system to fight off the cancer cells. They were instructed by the researchers to imagine the cancer cells, the working of the immunological system as represented by white blood cells and the fighting of the disease by whatever treatment they might be receiving.

The "mind pictures" and subsequent interviews with the patient about those drawings enabled the therapists to better understand how the patient felt about the disease, the process and the treatment. The imaging also enables the physician to understand the patient's attitudes toward the disease and the treatment and the patient's expectations. The two stress that the aim of such a program is cooperation with the treatment, not to be confused with a cure for the disease.

Achterberg is an assistant professor of physical medicine and rehabilitation at the health science center. Lawlis is associate professor of psychology at North Texas State University.



Dr. Jeanne Achterberg

Memorial for DeLoach

Memorial services were held on campus March 8 for Dr. Asa W. DeLoach, professor and former interim chairman of psychiatry. DeLoach, 56, died Feb. 15. The popular teacher and faculty leader had been active in Southwestern's psychiatry program until a few days before his death, despite failing health. A fund has been established at the center in his memory, for use in furthering the teaching of psychiatry.

Joint transplant

A rare surgical operation that involved transplanting part of a knee joint from a cadaver into a 60-year-old man whose knee had been ravaged by degenerative arthritis was performed by U.T. Southwestern surgeons last August.

The operation, which involves removing damaged bone and cartilage and then "resurfacing" the end of the bone with tissue from a cadaver, was done by Dr. Marvin H. Meyers, a pioneer in the development of the new surgical technique, and reduces or completely alleviates pain in joints destroyed by certain forms of arthritis.

Meyers, professor of orthopedic surgery, says the patient regains normal function of the joint although there still may be a small degree of limitation of motion.

Use of a cadaver joint instead of the plastic or metal devices commonly used offers several advantages, he says, including "buying time" for a younger, highly active patient by providing him with a number of years of good joint function. "We haven't burned our bridges behind us when we do one of these transplants," he adds. "If the graft fails when the patient is older and a better candidate for the artificial replacement, then an artificial joint can be substituted."

Treating impotence

Evidence that the master brain hormone LHRH may be useful in treating sexual impotence has been produced by two health science center researchers, Drs. Robert L. Moss and Samuel McCann. The scientists have demonstrated that LHRH (luteiniz-

ing hormone releasing hormone) stimulates sexual behavior in rats, and recent studies involving 50 men here and at several other laboratories indicate that it also may increase the sex drive in humans, although to a lesser degree.

Moss, associate professor of physiology, emphasized that LHRH is just an experimental drug that will probably help only those with "secondary" impotence. And studies indicate that the drug is effective only in patients who still have some level of sexual activity when they begin the drug therapy.

Moss and McCann, professor and chairman of physiology, head the Dallas research team. It was McCann who first found proof of LHRH's existence in 1960. Since then, two other peptide hormones produced by the same region of the brain have been discovered by researchers at other institutions.

Cholera vaccine

A vaccine which immunizes against cholera and a number of other diarrheal diseases may result from the isolation of the bacterial mutant "Texas Star." Dr. Richard A. Finkelstein, professor of microbiology, said he and his associates have finally succeeded in inducing genetic changes in the cholera bacterium so that it produces a harmless toxin while immunizing against the virulent form of the disease.

Dr. Takeshi Honda, a fellow in Finkelstein's laboratory, successfully isolated a mutation of cholera the group has named Texas Star. In animal experiments Texas Star produced no diarrhea yet caused formation of antibodies which neutralized toxins produced by *E. coli* and cholera. The new mutant may also be a weapon against "turista."

Finkelstein made the announcement during a Nobel Symposium in Stockholm, and said "Human trials could start at any time."

Beleaguered liver

The "good life" enjoyed by so many people in countries such as the United States may increasingly become a "short life" as the combined results of drugs, environmental pollutants, alcohol and disease wreak havoc on the hard-working but beleaguered organ, the liver.

To combat the expected rise in liver diseases — predicted to become the third leading cause of death within the next decade — Dr. Burton Combes and other liver experts have organized the American Liver Foundation. Combes is a prominent liver researcher and professor at the center.

"Our high standard of living is very hard on our livers," says Combes, who was named first chairman of the recently-formed organization. The purpose of the foundation is to develop support for research in liver disease, which Combes sees as becoming a serious problem for society, since death from liver diseases is often preceded by prolonged illness requiring frequent hospitalization.



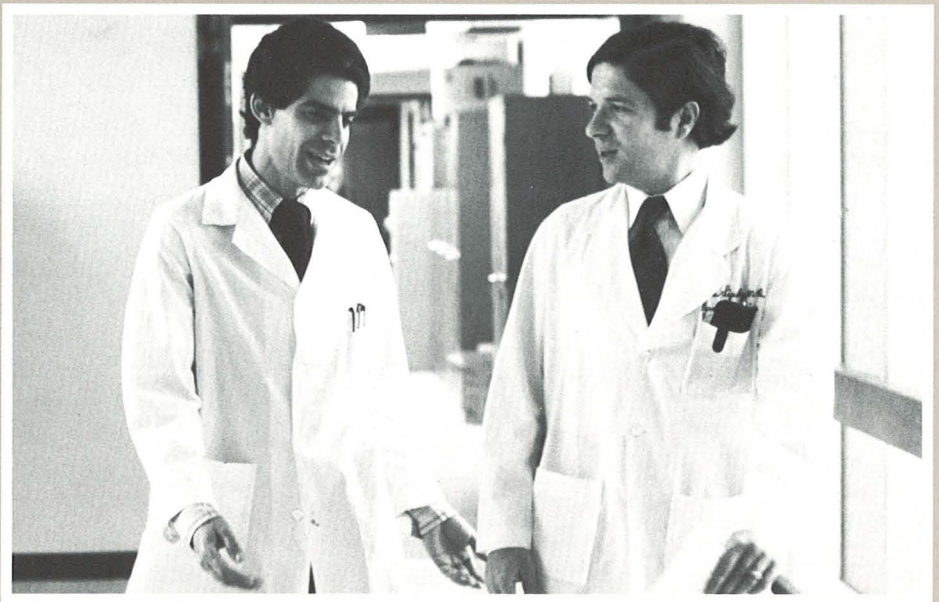
Dr. Ruth Guy

Guy steps down

Dr. Ruth Guy stepped down from her posts as chairman of the medical technology program and associate director of the Parkland Memorial Hospital Blood Bank to concentrate on her teaching duties and research. Dr. Guy, professor in both the Department of Pathology and the Department of Medical Technology, chaired the med tech program for nine years before relinquishing the post last fall.

The noted hematologist has also served as a consultant for the Southwestern Institute of Forensic Sciences, and has traveled all over the country assisting police and medical examiners in identification of blood stains after crimes have been committed — including the Juan Corona case in California, where she helped police attempt to learn the identities of the 25 murder victims.

As a symbolic "good-bye" gift, Guy has established an emergency student loan fund which she hopes others will continue to add to, remembering her own days as a graduate student when "I wouldn't have made it" had there not been emergency funds available.



Dr. Thomas Rogoff (left) and Dr. Peter Lipsky

Liver's immunity role

New proof that the liver has an active part in the body's immune system has been detailed in research by health science center fellow Dr. Thomas M. Rogoff.

In his research, Rogoff isolated Kupffer cells and discovered the role they play with blood lymphocytes, or white cells, in disposing of antigens, or foreign materials, in the liver. Rogoff, who was awarded the American Liver Foundation's first annual Research Prize for his work, presented his findings at the 29th annual meeting of the American Association for the Study of

Liver Diseases last November.

The liver has long been looked on as a chemical regulator, manufacturer and treatment plant, but Rogoff's work has shown that it also has an immunological function. Rogoff, who developed a method for isolating the Kupffer cells, confirmed that these cells work in a cooperative effort with lymphocytes, first processing foreign substances in the body, and then passing along signals about their presence to the lymphocytes, which are then capable of mounting an immune response to these materials.

Innovative orthotics

Former naval medical corpsman Mel Stills is the Center's new director of orthotics and prosthetics. Stills, who has been designing experimental orthotics and prostheses for 12 years, came to the health science center following a seven-year stint at the Research and Engineering Center associated with Moss Rehabilitation Hospital and Temple University, both in Philadelphia.

Stills' innovative designs in orthotics have enabled patients to go from heavy steel-and-leather braces to the new lightweight plastics, which conform to the shape of the leg and weigh as little as four ounces. A boon particularly for small children, the devices enable the wearer to enjoy stylish boots and shoes instead of heavy, unsightly orthopedic shoes.

In addition to his duties at the health science center, where he has set up a laboratory to work for patients referred to orthopedic surgery, he is also involved with orthopedic patients at Scottish Rite Hospital and Caruth Rehabilitation Center.

He sees professional education as a top priority. "Physicians are interested in learning about better fitting procedures and new devices for their patients. There simply has not been this knowledge available in this part of the country up to now," he says.

Goth honored

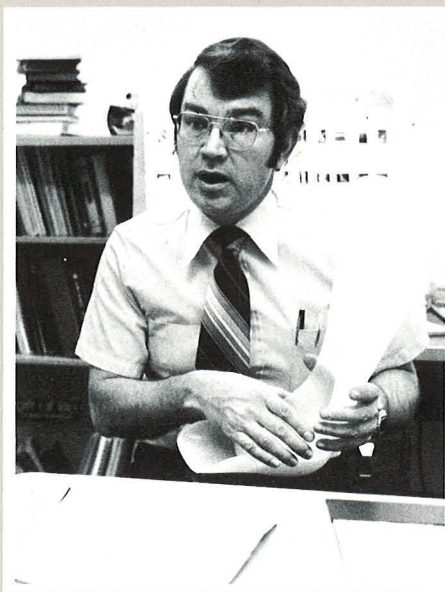
Southwestern Medical School alumni were to present double honors at their annual banquet May 3. As Dr. Andres Goth, Southwestern's senior department chairman, neared the end of his tenure as head of Pharmacology, graduates planned to pay him tribute and to surprise President Charles C. Sprague with a "roast" in the form of "This Is Your Life" in honor of his ten years as president.

Goth joined the medical school in 1944 and was named chairman of Pharmacology in 1950. During his tenure as administrator, he has earned the respect of his colleagues for his grasp of the total spectrum of the science of pharmacology. He is working on the ninth edition of his textbook "Medical Pharmacology," which in the two decades of its existence has sold over 300,000 copies and been translated into at least eight languages.

Alcoholic rats

"Teetotaling" rats are being turned on to alcohol in an effort to determine the cause of a little-known complication of alcoholism — the breakdown of skeletal muscle.

Research into alcoholic myopathy, the muscle destruction that occurs in most and possibly all chronic alcoholics, is being done by Dr. James Knochel, professor of internal medicine. Several years ago, Knochel, chief of research at the Dallas Veterans Administration Hospital, observed that a very large number of alcoholics at the hospital were developing dangerously low levels of phosphorus in their blood within two or three days after admittance



Mel Stills

to the hospital. Phosphorus is an essential part of the chemical compound ATP, which is the ultimate source of energy for every cell in the body. Deprived of phosphorus, muscle cells literally "fall apart," spilling their contents into the bloodstream.

Muscle damage observed in sufferers of alcoholic myopathy has been duplicated by UT researcher Dr. Ron Haller in rats by taking phosphorus out of their diet, and it was found the rats could be "cured" simply by putting phosphorus back.

Knochel hopes to determine through his research on "drunk" rats why hospitalized alcoholics lose phosphorus and if supplementing their diet with phosphorus can prevent the muscle breakdown.

'Back' to school

Victims of chronic back pain are "drawing" their pain under the guidance of Dr. Vert Mooney, head of orthopedic surgery — giving the physician a much clearer understanding of the patient's problem and the extent of pain the patient is suffering. This is just one of the unorthodox approaches Mooney uses in waging the war against chronic pain. His patients — many of whom are survivors of multiple surgeries — are also sent back to school.

Initially, the surgeon's patients are asked to describe their pain through symbols drawn on a paper doll-like form. This gives Mooney vital information about not only the pain, but the patient's degree of emotional involvement with it.

Continuing this mind-body approach to spine-related pain, he often refers his patients to "pain schools" where they learn pain management techniques such as exercises, body mechanics to keep their backs from getting worse, and relaxation techniques. The idea is to de-emphasize pain and help the patient master techniques for managing pain that they can use for the rest of their lives — a program that in-

volves not only the patient and health team, but family as well.

"The old attitude — if you can't operate on it or can't give it medicine, it's not worth talking about — is dying out," says Mooney. "The total health care approach to pain is as much a frontier today as cardiac catheterization was yesterday."

Glucagon and diabetes

New and convincing evidence that the controversial hormone glucagon is important in diabetes has been presented by Dr. Roger Unger, professor, and Dr. Philip Raskin, associate professor, Department of Internal Medicine. Their report, the lead article in the Aug. 31 issue of "New England Journal of Medicine," may resolve a major medical controversy — one with implications for millions of diabetics.

Although glucagon was discovered in 1923, it was not until Unger's pioneering research that the potential significance of glucagon in diabetes began to be recognized. His work indicated that an excess of glucagon, as well as a lack of insulin, might be involved in diabetes, which up to then had been considered a "unihormonal" disorder.

The new study demonstrates that an abnormally high level of glucagon is significant in diabetes and that correcting the excess of glucagon brings the diabetic's blood sugar level back to or towards normal.

In March, Unger was named "Senior Medical Investigator" by the Veterans Administration for his work on diabetes. Only 11 researchers nationwide have been appointed to this position since the awards program began in 1959.

Telltale syndrome

A study of a heart condition known as mitral valve prolapse may affect the treatment of women labeled "neurotic" because they exhibit classic symptoms of hysteria. Drs. Drew Gaffney and Gunnar Blomqvist are studying the heart condition in young women, who have the same symptoms often associated with hysteria — chest pains, palpitations, shortness of breath, anxiety, dizziness or fainting spells and excessive fatigue. Their contention is that many women treated for anxiety and hysteria, with tranquilizing drugs both in hospital emergency rooms and doctor's offices, may in fact suffer from the mitral valve prolapse syndrome.

The condition, says Gaffney, internal medicine instructor, is "very difficult to diagnose at times, even for experienced physicians. The one telltale sign or signature of the syndrome, the sound of a 'click' followed by a murmur of the heart, isn't always present."

The two doctors believe physical training on a regular basis may be the answer for some of these patients.

But the condition can sometimes be provoked by certain procedures so the physician who suspects mitral valve syndrome should put the patient through a series of

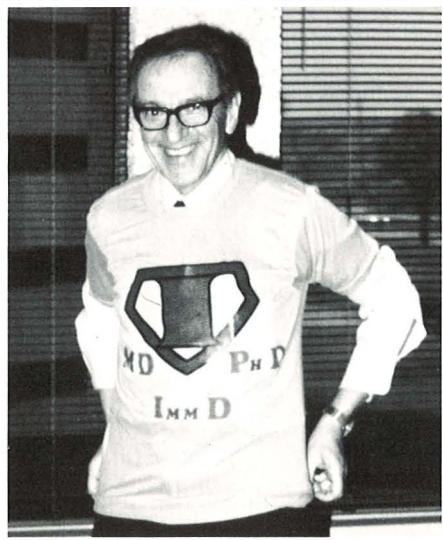
exercises while listening to her heart.

Ziff gets an 'Imm.D.'

The first "Imm.D." was presented to Dr. Morris Ziff, professor of internal medicine, by his immunology co-workers and students. The Mice and Hamster people gathered on Groundhog Day to toast and roast "the primordial immunologist." In a celebration typical of the group, Ziff was presented the usual piece of paper and also the "Super I" T-shirt.

Ziff, who celebrated his twentieth anniversary at the health science center last year, recalled his early days at the center when the immunologists had one small office and a small darkroom near the men's room that he called the "paratilet."

"In the early days, I never would have dreamed this gathering of immunologists and students possible," he commented, referring to the crowd of nearly 100 who came to pay him tribute and poke a little fun.



Dr. Morris Ziff

Newsmakers

Dr. Vernie A. Stembridge, chairman of the Department of Pathology and president of the American Society of Clinical Pathologists, was honored by The University of Texas at El Paso as Outstanding Ex-Student during homecoming in October, 1978. Stembridge has been a member of the pathology faculty since 1959, serves as director of the Tumor Clinic at Parkland Hospital, and is a trustee of the American Board of Pathology.

For his contribution to better understanding of the body's absorption processes, **Dr. John M. Dietschy**, professor of internal medicine, was awarded the 1978 Distinguished Achievement Award of the American Gastroenterological Association.

Dietschy was cited for his "major specific accomplishment in gastroenterology," including the clarification of a very funda-

mental concept of transport, the mechanisms whereby all sorts of food substances get absorbed across the small and large intestine. Said Dr. John S. Fordtran, chief of gastroenterology, "Dr. Dietschy's findings have importance in all fields of biology and medicine, not only in the gastroenterological tract but in the kidney, stomach, bladder — all organs that absorb or secrete." His findings are important, too, in understanding previously unknown causes of digestive dysfunction, such as may occur in diabetes, collagen disorders and certain neurological diseases, and after some forms of surgery.

Dr. A. H. Giesecke, Jr., vice-chairman of the Department of Anesthesiology, was named to the M. T. Pepper Jenkins Professorship in November. The Jenkins professorship was endowed by Mrs. Eugene McDermott. Dr. Jenkins has been chairman of anesthesiology at the health science center since 1951, and has held the Margaret Milam McDermott Chair in Anesthesiology since the McDermotts established the chair in 1966.

Dr. Giesecke, who was first associated with the department as a resident at Parkland Memorial Hospital in 1960, assumed his post as vice-chairman at the center in 1974 after serving as professor and director of the anesthesiology program at The University of Texas Health Science Center at Houston.

Dr. Denis McGarry was named the 1978 recipient of the Lilly Award for outstanding research in diabetes as a result of his research into the problem of the mechanism of ketone body production in starvation and in diabetes.

McGarry, professor of internal medicine and biochemistry, said that "after taking every bottle off the shelf" and looking at every metabolic step in the liver's oxidation of fat and coming up empty-handed, he decided to look at the opposite metabolic pathway. The result? The discovery that malonyl-CoA shuts down the production of ketone bodies. Glucagon appears to reduce

the concentration of malonyl-CoA in the liver, with the result that ketone body production is accelerated.

The Lilly Award is presented annually by the American Diabetes Association to an investigator under the age of 40.

Drs. Michael S. Brown and Joseph L. Goldstein were named co-recipients of the 1978 Passano Award, presented "in recognition of the brilliant work which unraveled the heretofore impenetrable yarn of blood cholesterol at levels of molecular physiology, human pathology and genetics."

Goldstein is chairman of the Department of Biophysics and Molecular Genetics and Brown is director of the Center for Genetic Disease in that department. The two are also designated as Paul J. Thomas Professors at the medical school.

Of the 300 most frequently cited researchers in the life sciences during the period 1961-76, 12 are affiliated with Texas institutions. Five of that elite group are at the Dallas health science center.

The list appeared in "Current Contents," published by the Institute for Scientific Information. The five faculty members on the list are: **Dr. Ronald W. Estabrook**, Virginia Lazenby O'Hara Professor and chairman of biochemistry; **Dr. Samuel M. McCann**, professor and chairman of physiology; **Dr. Roger H. Unger**, professor of internal medicine; **Dr. Jonathan W. Uhr**, professor and chairman of microbiology, and **Dr. Jean D. Wilson**, professor of internal medicine and director of the Eugene McDermott Center for the Study of Human Growth and Development.

Dr. Eugene Garfield, founder and president of ISI, explained the "most cited" list: "If an author is consistently cited, indeed thousands of times over a number of years, this record indicates (with occasional exceptions) that he or she has made a significant impact on science."

— Compiled by Susan Wilson

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