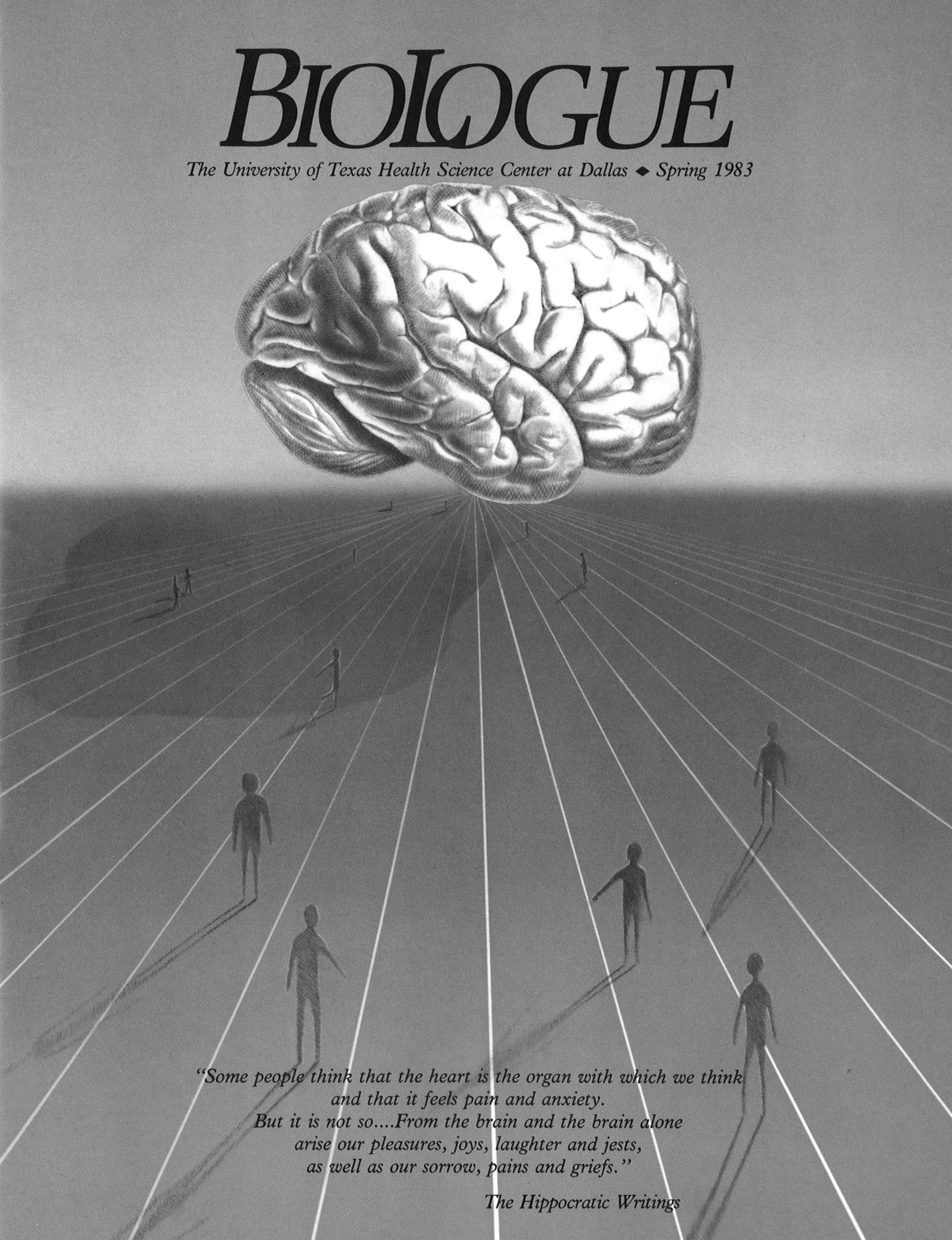
BIOLOGUE

The University of Texas Health Science Center at Dallas ◆ Spring 1983



"Some people think that the heart is the organ with which we think
and that it feels pain and anxiety.
But it is not so....From the brain and the brain alone
arise our pleasures, joys, laughter and jests,
as well as our sorrow, pains and griefs."

The Hippocratic Writings

Editor's Message

The brain is no longer sacrosanct. Researchers are spying on the living brain as it functions in the body or on individual cells and what proteins they are producing. Clinicians are using the latest technology for diagnosis and treatment of physical mental disorders. And the brain is gradually giving up its secrets.

Using our brains to write about researchers using their brains to study the brain has a dizzying effect. It's like looking at a mirror reflection in a mirror in a mirror....

We hope this issue of *BioLogue* boggles your mind – at least a little. Maybe a neuron or two will be excited and produce an extra supply of endorphins. That could be what mind-boggling is all about.

Ann Williams

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Editor

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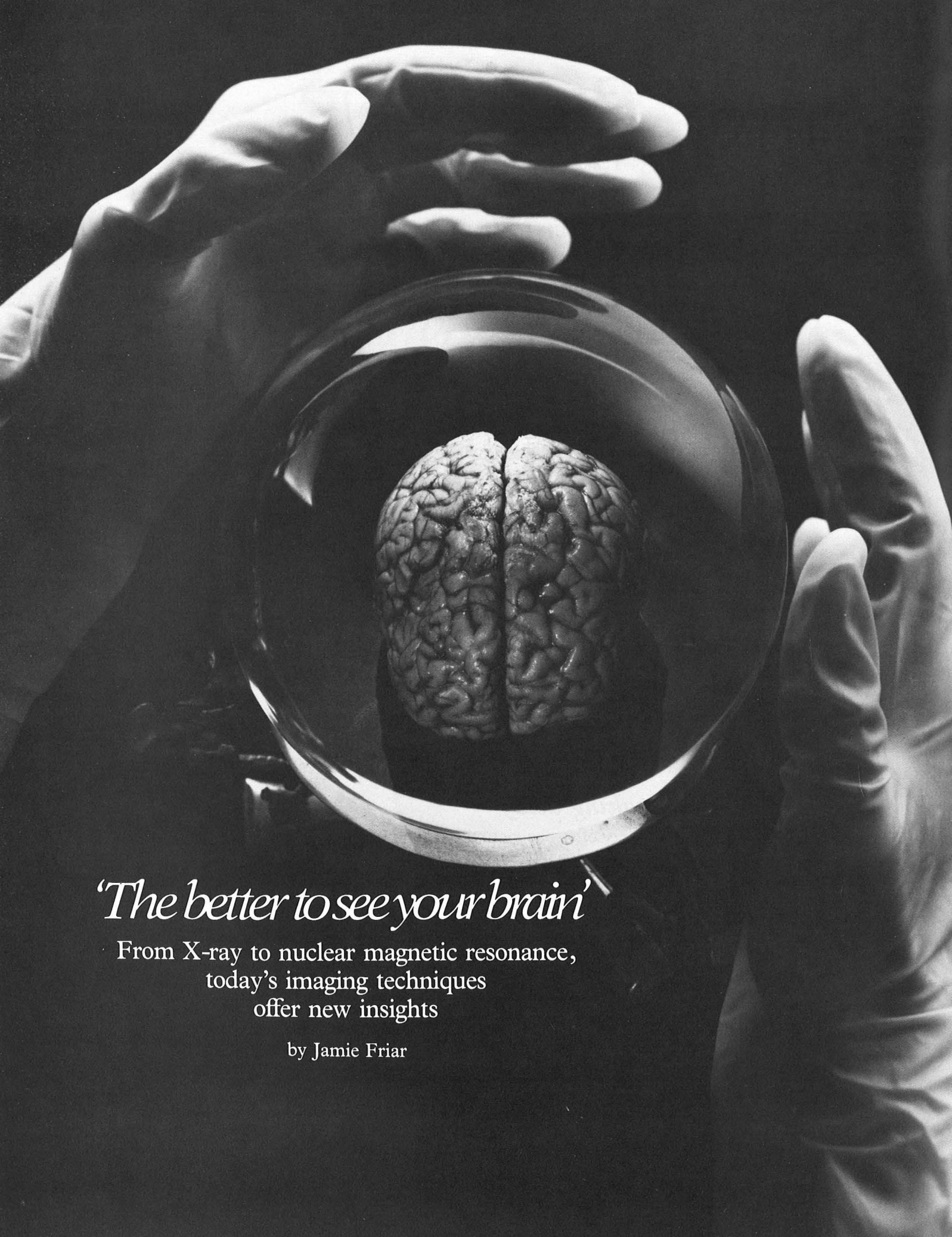

'The better to see your brain'

From X-ray to nuclear magnetic resonance, today's imaging techniques offer new insights

by Jamie Friar

The quest for exploration has led to every corner of the world. We have reached out to the planets and the stars. Now science is probing a mysterious gray world, boundless as the universe but weighing just three pounds...the human brain. Physicians and scientists have marshalled an impressive array of imaging technologies that allow them to peer inside the head and actually view the brain as it functions.

All imaging techniques, from the simple X-ray to the sophisticated computerized tomograph (CT) share the same goal. "Diagnostic imaging is an attempt to determine either pathology or physiology inside the patient with the least risk to the patient," said Dr. Robert Parkey, chairman of Radiology at The University of Texas Health Science Center at Dallas. To accomplish the goal of minimum risk the physician and the research scientist are improving techniques and developing new imaging technologies.

Humans have always been fascinated by what happens inside the head. Aristotle speculated on the source of human emotions and the integration of mind and body. Hippocrates noted that epilepsy was not a sacred disease, "but has a natural cause from which it originates." Andreas Vesalius, the great Renaissance anatomist, detailed the central nervous system.

X-ray

It was not until the late 19th century however, that a burgeoning modern science created a method that allowed us to look inside the head of a living being. A ray was discovered that could pass through flesh and bone. As yet unnamed, it was dubbed the "X" ray in 1895 by its discoverer Wilhelm Konrad Roentgen. Roentgen was a physicist, not a physician. He had little interest in the use of the X-ray as a medical tool but did recognize its potential. He invited other scientists to pursue the clinical uses of the X-ray. Roentgen did not patent his discovery and freely published his findings so others could continue work on the mysterious ray.

Dr. Harvey Cushing, the father of neurosurgery, had entered his year of internship at Massachusetts General Hospital in 1895, the year the X-ray was discovered. He was among the first to use the technique in the Boston area, and to X-ray the human skull. The visualization X-rays provided of the skull were fundamental in the development of neurosurgery pioneered by Cushing.

An X-ray is a shadowgram. The rays pass through substances with varying degrees of absorption. X-rays are only slightly absorbed by flesh and soft tissue. Bone and other dense material absorb a greater amount of the radiation, leaving a white shadow on the X-ray plate. Today many of our modern imaging technologies rely on the very basic nature of X-rays and the absorption rates of differing biological materials.

X-rays as an imaging method have their limitations. While it is easy to visualize defects in bone structure (i.e., a skull fracture), disease or damage in softer tissues is more difficult to see, and prolonged or repeated exposure may be hazardous.

Angiography

One refinement of basic X-ray technique is the use of a contrast medium. Soft tissues and structures, if filled with or surrounded by material opaque to X-rays, will be visible on the X-ray plate. Following World War II, angiography was introduced.

To visualize the blood vessels of the brain, a catheter inserted in the femoral artery is threaded through the arterial system, including the heart's aorta, and placed in the carotid artery. An iodinated contrast medium is injected directly into the carotid. Iodine, opaque to X-rays, clearly outlines the cerebral vascular system.

"I can't imagine anyone opening up someone's head without an angiogram or CT scan," said Parkey. "You wouldn't know where the vessels are coming from, where the nasty (blood) feeders are. It would be back to Egyptian times if you opened a head without an angiogram."

Angiography is the definitive study for a variety of cerebral vascular disorders such as aneurysm (weakened blood vessel), arteriovenous malformation (deformed or tangled vessels) and arteritis (chronic inflammation of large arteries).

While angiography has proved to be a useful diagnostic resource, it does carry some risk and physicians are cautious to order the procedure. Angiography is considered an invasive process because a catheter is threaded through vital arteries. There is a possibility that blood supply to a vital organ may be disrupted or that the procedure could trigger a stroke or heart attack. Allergic reactions to the contrast medium must also be considered. A major disadvantage to the iodinated media is the variable and unpredictable occurrence of such reactions. The complications can vary from slight to life-threatening.

Unfortunately, there seem to be few signs that may aid the physicians in predicting which patients may have adverse reactions. Considering the potential for complication, angiography is performed in a clinic or hospital setting where there are adequate emergency facilities. According to Parkey, "Angiography is hazardous stuff – it is the last thing on your list."

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Brain Scan

Until the World War II atomic bomb program let the nuclear genie out of the bottle, the field of nuclear medicine was virtually non-existent. Now nuclear medicine technologies play a prominent role in brain imaging – past, present and future.

Brain scanning with radioactive substances relies on the phenomenon of the blood-brain barrier, according to Dr. Frederick Bonte, a pioneer in the field and director of the Nuclear Medicine Center. The brain's blood vessels have a natural filter that keeps out noxious agents that may be circulating through the bloodstream. The blood-brain barrier allows only the substances needed for brain functioning to pass. This natural filter tends to break down when tumors or other pathologies are present. The phenomenon allows radio-

CT scan

pharmaceuticals circulating in the blood to leave the vessels in the diseased areas and enter the substance of the brain, said Bonte.

In the late 1940s primitive radiation detectors (Geiger counter - like devices) were simply held up to the patient's head and the flow of radioactively tagged blood was followed. Later years saw the development of scintillation counters that allowed an image to be displayed on a screen. Today relatively few brain scans are performed, having been supplanted by the more detailed computerized tomography (CT or CAT) scans.

Computer

The huge memories and data processing power of the computer have led to a revolution in medical imaging. Coupled with X-rays, nuclear medicine techniques and even magnetic fields, the advances of computer science give physicians new tools to see with. "The bottom line is finding out what's wrong with the patient," said Parkey. "In the old days you listened, you felt and then you guessed. The smarter you were, the better your guess. The reason imaging technology has revolutionized medicine is that it makes the diagnosis so much more accurate."

Today's advanced imaging devices do not yield a sheet of film that one can hold up to the light for viewing. Now microcircuits and computer memories are needed to store and process the vast amount of information needed to produce a single image. According to UTHSCD computer scientist Dr. Meg Lewis, "The computer today is an integral part of modern image processing."

CT Scan

X-rays coupled with the data processing power of computers and microcircuits have led to computerized tomography. "It has given us a completely new way to look at the patient," according to Dr. Kenneth Maravilla, associate professor of Radiology. Application of the CT scan technique reveals "information that before was not obtainable prior to death and autopsy."

The CT scanner makes use of an imaging method used since the 1930s but incorporates sophisticated modifications only made practical by the advent of high speed data processing. The image produced by CT is a tomograph, the depiction of a single cross-sectional plane. Unlike a conventional X-ray, the CT scanner can distinguish structures and surrounding space in three dimensions.

The scanner sweeps a highly focused X-ray beam across the section of the body to be imaged. Sensitive detectors record the amount of X-ray absorbed by the body as the beam circles 360 degrees. A computer stores and processes data on minute changes in absorption in different tissues of the body. After hundreds of thousands of calculations, which can be completed in seconds, the computer displays the resulting image on a TV-like screen. The cross-sectional image of a human head appears as though you were looking down on a front-to-back slice. You can clearly see the various anatomical landmarks that would be indistinguishable on a conventional X-ray.

In the late 1940s primitive radiation detectors (Geiger counter - like devices) were simply held up to the patient's head, and the flow of radioactively tagged blood was followed.

CT found its first application in visualizing abnormalities of the brain. In fact, the first patient ever to be scanned was a woman with a suspected brain lesion. The scanners are very sensitive to minute changes in X-ray absorption and can even reveal differences

in the gray and white matter of the human brain. Such soft tissue disorders as tumors, swelling and bleeding can be readily seen on the CT scan. Virtually all medical problems involving the head and brain today entail a CT scan as part of the diagnostic procedure.

CT scans, like conventional X-rays, can be enhanced by injection of a contrast medium for visualization of vascular structures and abnormalities. But unlike the angiogram, no catheter is needed. A contrast agent circulating in the bloodstream will not penetrate the vessels of normal brain tissue, while a breakdown in the blood-brain barrier will allow the "dye" to leak into the diseased areas. A subsequent CT scan reveals the blood vessels in the damaged area in great detail.

CT is considered a non-invasive technique without significant risk or discomfort to the patient. As in all X-ray procedures, precautions are taken to minimize radiation exposure to staff and patients. Perhaps the one drawback of CT is the high cost of the equipment, $1 million scanners are the norm rather than the exception.

The rapid advance of CT finds few parallels in medicine. The first human scans were performed in 1972. The early scanners of a decade ago could visualize structures of approximately 130 cubic millimeters, about the size of a pinto bean. Today's scanners have increased that resolution more than 100-fold, according to Maravilla. The first scanners took up to 20 minutes to reconstruct an image; today's devices take seconds. In just 10 years the CT scanner has gone from the laboratory to everyday medical practice.

Parkland and UTHSCD now have three CT scanners. Maravilla and his staff have performed more than 20,000 head scans alone. Research conducted here has led to a refinement of CT technique and better interpretation of results.

The CT scanners and other imaging techniques discussed thus far tell us much about the structure of the head and brain, but little about brain function. A new imaging modality being researched at UTHSCD's Nuclear Medicine Center holds great promise for revealing how specific areas of the brain are related to various neurological tasks.

Emission Tomography

Bonte and his colleagues are perfecting an imaging method known as single photon emission tomography. Unlike CT, X-rays are not used. In their place, electronic detectors sensitive to very slight radioactive emissions form the basis of the imaging device. UTHSCD's emission tomograph (ET) is one of only a half dozen similar machines in the world. It is being used to study blood flow in the brain.

The patient inhales a small amount of radioactive gas that is absorbed by the blood. The ET senses the radioactivity as the tagged blood flows through the brain. Scintillation counters detect the location of the emissions, and a computer records the position data. A tomographic slice depicting brain blood flow in a color-coded image is displayed on a computer screen. Disruption of blood flow to certain areas of the brain is associated with disease.

Areas of the brain used in various mental processes can also be seen on the ET screen. When a test subject is looking at a photograph, brain areas used for vision light up. If the subject attempts to solve a math problem, the area of the cerebrum associated with cognitive thought is visualized.

Bonte said when the field of nuclear medicine first opened up, no one had any idea the discipline would advance as rapidly as it has. Years ago Bonte and a colleague tried to build a simple box camera to record the image of a bottle filled with radioactive material. A fuzzy image was cause for celebration. Today detailed imaging of the brain and other organs is no longer a longed-for goal, but a reality.

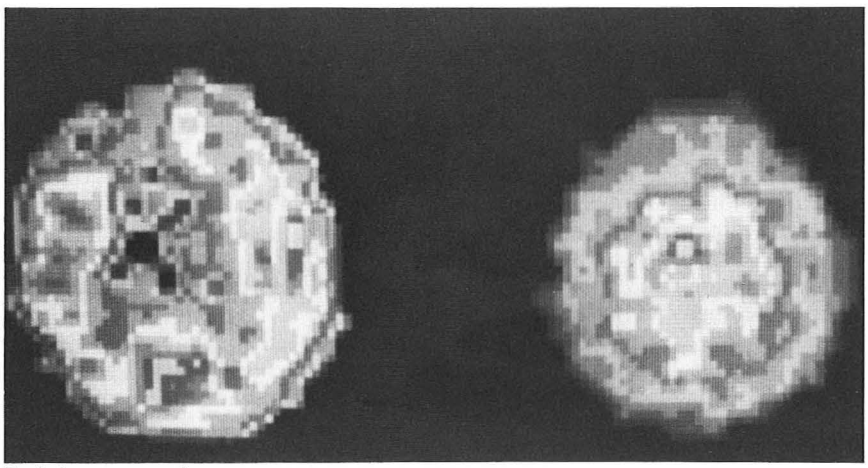
The early scanners of a decade ago could visualize structures of approximately 130 cubic millimeters, about the size of a pinto bean.

Nuclear Magnetic Resonance

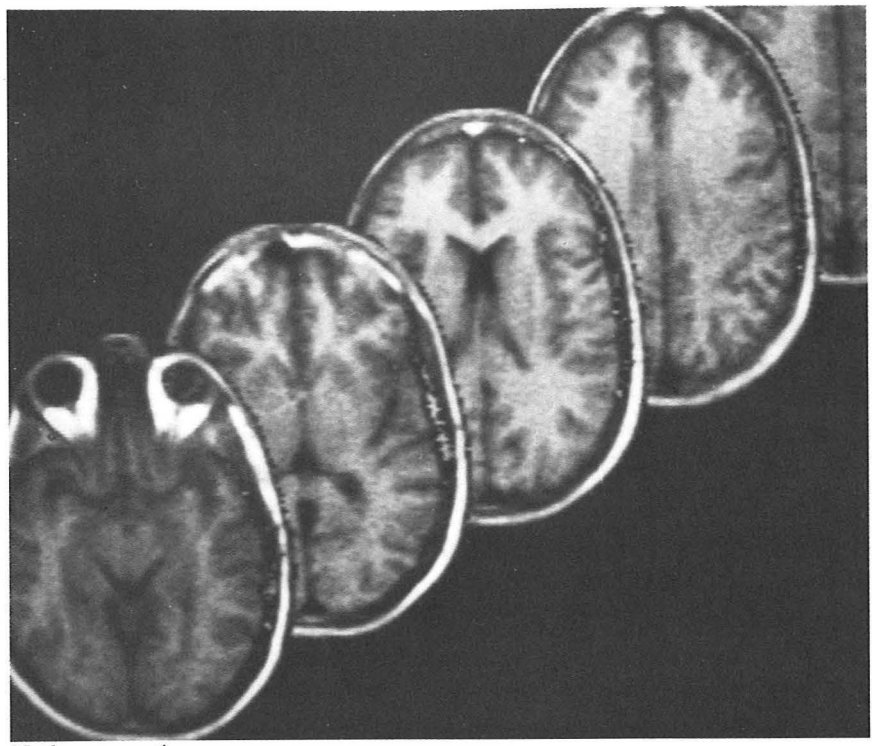
Another of the newest imaging tools has as its foundation another basic force of nature – magnetism. Nuclear magnetic resonance imaging relies on neither radioactive material nor X-rays but takes advantage of the magnetic properties of certain elements. NMR holds great promise for imaging as well as the measurement of metabolic function.

The nuclei of all atoms contain protons and neutrons (with the exception of hydrogen, which consists of a single proton). When the nucleus contains an unpaired proton or neutron, it is possible to induce it to spin in the presence of a magnetic field. NMR uses powerful superconducting magnets to line up the nuclei along a north/south axis, as if the atoms were tiny bar magnets in a strong magnetic field. The elements most often detected in NMR are hydrogen, phosphorus and a minor carbon isotope.

A radio pulse is then transmitted



Emission tomography



Nuclear magnetic resonance

that causes the aligned nuclei to wobble or spin off axis. When the radio frequency pulse is turned off, the spinning nuclei gradually return to their equilibrium or "on axis" position. As they move back to their original position, the wobbling nuclei will resonate a radio frequency that is picked up in an antenna-like coil.

The principles of NMR can be applied to either imaging or spectrometry. Individual elements will resonate at specific frequencies. By changing the frequency of the radio pulse, the elemental composition of material can be determined.

For imaging, the intensity of the magnetic field is modulated. A change in the strength of the field will result in a corresponding change in the frequency of the resonated radio pulse. This fundamental axiom of NMR, that the intensity of the magnetic field is proportional to the resonated radio frequency, makes it possible to locate the spinning nuclei in three-dimensional space. A series of sequential magnetic gradients of varying strength are lined up to determine the position of material being imaged. A computer stores the position data and reconstructs a tomographic image.

NMR used for imaging has much in common with CT, but there are some distinct differences. As in the early days of CT, much of the NMR imaging being done today is on the head and brain. That is due partly to the size of the available machines. The UTHSCD research NMR unit has a 12-inch aperture, large enough for a limb or head but not for the whole body. (A whole body NMR unit is expected this spring.)

NMR, like CT, is a tomographic imaging technique offering "slice" views of the body. Unlike CT, the NMR can offer a slice from any angle not just the axial view. NMR images of the skull and brain may be taken from the profile perspective, impossible with CT. The NMR unit records and stores all imaging information in one pass. If physicians want to see a "slice" from another angle, they just have to instruct the computer which perspective they would like to view. The NMR computer contains the data for a fully three-dimensional image, but as of yet the technology does not exist to display such a 3-D view.

NMR offers the advantage of perhaps being able to detect a disease state before there are any clinical manifestations. That possibility is particularly exciting to Dr. Ray Nunnally, assistant professor of Radiology. "There are these so-called promoter states for certain types of cancer where the cells are not yet cancerous but they have definitely changed from their normal state." Nunnally believes that NMR may be able to detect metabolic changes on a cellular level "before the cells are ready to go wild." He can foresee the day when an NMR scan would indicate that a woman is at risk of developing breast cancer or that a patient has an early stage of heart disease.

Nunnally said NMR imaging has a variety of clinical uses in head injuries and neurological disorders, "virtually anything you can use any current diagnostic imaging technique for."

Science fiction fans will be familiar with the device that is passed over the patient and all his ills are instantly diagnosed. "We're far, far from that, but that's the direction we're moving."

NMR imaging can distinguish between healthy tissue and diseased tissue. The diseased cells have a distinct magnetic resonance when compared with their healthy counterparts, and the NMR computer can be programmed to display the diseased areas, a feat not possible with other imaging methods.

Nunnally said current research indicates that NMR does not have any known hazards.

Science fiction fans will be familiar with the device that is passed over the patient and all his ills are instantly diagnosed. "We're far, far from that," says Nunnally, "but that's the direction we're moving."

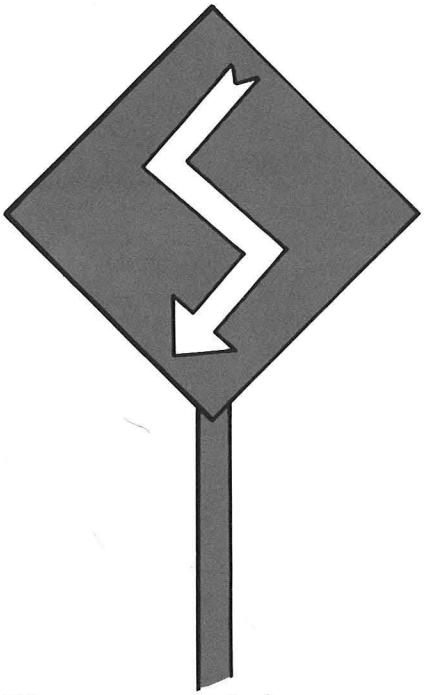
The Future

During the last few decades great strides have been made in the field of medical imaging, and our ability to view the brain in particular. Today we can visualize the gray and white matter of the brain, view tumors and other disease states, see blood flow and metabolic function. All were impossible just a few years ago. In spite of all the technological advances, researchers have not become complacent. They still have visions. Said Bonte, "We'd like to visualize each and every cellular process and to localize what we see to the smallest possible volume. We're a long way from doing that." ♦

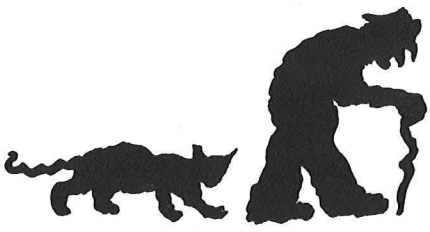
Getting it straight

Children with psychiatric problems can benefit from short-term hospital care at Children's Medical Center

by Ann Harrell



There was a crooked man,
and he went a crooked mile,
He found a crooked sixpence
beside a crooked stile;
He bought a crooked cat,
which caught a crooked mouse,
And they all lived together
in a little crooked house.



Sometimes the whole world appears warped to people who are having emotional problems – depression, anxiety, panic, hysterical outbursts. This "crooked world" that they perceive may be a terrifying place, and their own terror often brings them to seek help for the distortions of their own minds. Fortunately, most are adults who can say to themselves, "I'm hurting. I need help."

Unfortunately, many are not able to realize that something is wrong in their world. They may be frightened by their own out-of-control feelings or confused by their warped perceptions. In most cases, they cannot verbalize the things that are going wrong.

"Children are not likely to come asking for help," says Dr. Kenneth Wiggins, chief of the Child and Adolescent Division and professor of Clinical Psychiatry at The University of Texas Health Science Center at Dallas. "A child is almost always brought in by somebody else. He or she is almost always doing something an adult doesn't want him to or not doing something the adult wants him to do."

But that doesn't mean that the child is not hurting. In cases like these, children simply do not have the vocabulary, maturity or self-understanding to know that something is wrong – or that they can be helped.

Nor can it be supposed that treatment for emotional disorders in children can, or even should, be just like that for adults, says Wiggins. With an adult, the psychotherapist generally aims at restoring the adult to a previous level of control or satisfaction in life. Children may never have learned or developed life skills to help them master the day-to-day environment. These skills may include relating to others, the ability to test reality, impulse control, learning to trust and a confident sense of self. With certain neurological disabilities, children may have had difficulty even in learning to read, spell or deal with numbers.

The problems of some children that result in their "crooked" views of the world or "crooked" ways of relating to it are complicated by the fact that they live in "crooked" homes where the parents need help, too. Sometimes the illness involves the whole family as in the case of the asthmatic child who starts wheezing whenever Mother and Father begin to fight. Thus the illness has a role in everyone's lives.

A child or young person with a major physical disease, such as acute diabetes mellitus or a severe seizure disorder, may be overwhelmed by depression, even to the point of becoming suicidal. There may be problems due to the patient's medication. Also, behaviors that help people cope with life have never been learned by the patient, who has not spent much time with other children during the growing-up years. Other young people may develop physical illnesses as a reaction to the emotional disorders they are suffering from or as a way of defending themselves from the world by becoming invalids. Therefore, an acute care pediatric hospital is the ideal place for a psychiatric unit that treats these special medically related problems as well as other psychiatric disorders.

Besides the outpatient psychotherapy program in the Child and Adolescent Clinic, the Department of Psychiatry has developed a special short-term inpatient psychiatric program at Children's Medical Center for cases where in-depth diagnosis and treatment are called for. Children's is a hospital for acute care for children and is the major pediatric teaching hospital for UTHSCD. The hospital is physically linked to the medical school.

The inpatient hospital program at Children's, says Director Dr. Graham Emslie, a pediatric psychiatrist, is one of the few in the country that provide care for children whose psychiatric disorders are due to or closely associated with acute physical disease. Patients with behavior disorders, other psychosomatic illnesses (such as some cases of asthma) and emotional disorders like depression, which has only recently been recognized in children, are also cared for here.

"Fortunately, the need for hospitalization doesn't come up very often," says Wiggins. "By far most children are normal – and even those with problems rarely need to be in a hospital. We are very aware of the disadvantages of hospitalizing children and taking them away from the family. But sometimes it needs to be done."

Out of every 100 pediatric patients seen in the hospital for physical illness, about 75 can be handled without any special therapeutic help; others need only a little special attention, say from an understanding nurse, says Emslie. Maybe 20 percent need to consult a therapist, just for one visit. And a small number – between one and five percent of the children in the pediatric hospital – have severe and complex enough problems that an inpatient evaluation in the unit is needed.

"It is to help that small percent who have enormous problems that we are here."

Some of these patients include young people like Wade, a 12-year-old boy born with an immunological deficiency that leaves him extremely vulnerable to infectious diseases and with a poor prognosis.

The problems of some children are complicated by the fact that they live in "crooked" homes where the parents need help, too.

Because of his illness, Wade has experienced a very limited childhood. He has missed a lot of school and has limited social contact with children his own age. He has to take large, painful shots of gamma globulin every two weeks and cannot participate in sports or other rough-and-rowdy games. He was admitted to Children's when his parents became concerned that their son was suicidal. Wade had "accidentally" shot holes in the living room floor while playing with his father's gun collection.

"My sister must have put the bullets back in when I wasn't looking," he said.

After several weeks, Wade is getting along well with the other children and teenagers, doing well with his school work and taking better care of himself. And he is able to deal with thoughts of his own death. Although he can't play football, he can go on nature walks, exercise in gym class in the unit, swim and participate in all the group excursions. The staff, especially child-care worker Eugene Kennedy, keep a watchful eye on Wade to keep him from overtiring. Kennedy, whom the kids call "Mr. Goo," often drops back to walk with Wade so he won't seem so far behind. And since Mr. Goo is a former TCU and professional basketball player, the kids think it's all right to slow down every now and then.

Patients come to the 16-bed unit from all kinds of backgrounds. Many are transferred from medical areas in the hospital as soon as their acute disease problems are stabilized; others are referred by local pediatricians or psychiatrists. Some are sent from local emergency rooms following drug overdoses or suicide attempts. About 50 percent of the patients have psychiatric problems closely related to diseases. Last year 66 patients were treated in the inpatient program.

Dr. David Waller, associate professor of Psychiatry and Pediatrics, is a psychiatric specialist in psychosomatic disorders in children and young people. Waller, who is head of the psychiatric liaison program at Children's, is present at all medical intake rounds with attending physicians. In this way he is able to help the other specialists spot children with acute medical problems who might need help with their emotional problems. In his role as consultant, he is able to get acquainted with the patient and the family and talk with them about the possibility of a psychiatric referral to the unit or outpatient therapy in a non-threatening way.

"People must be comfortable with the subject of access to psychiatric help," Waller says. "You can't just refer to the psychiatric unit like a medical area in the hospital, or you may get reactions from family members like 'Are you saying I'm a bad parent?' or 'Are you saying my child is crazy?' These parents may be feeling a lot of guilt about their child. You have to get to know them first in order to help."

Emslie agrees.

"The family," he says, "is a very important part of our program, and we can't help the child without their cooperation.

"We are a goal-oriented program, and that goal is to enable the child to function at home and in his community. We like to involve the families as much as possible. After all, the kids return to their families. In fact, weekly family therapy is a part of the program, and patients are allowed weekend visits

home," says the program director.

Besides family therapy, treatment plans may include medication, such as anti-depressant drugs; psychotherapy and behavioral techniques, such as behavior modification. In each case the treatment is individually tailored to the patient's needs.

Depression is a common problem seen in the psychiatric unit at Children's. Johnny, a slender 14-year-old, had to be readmitted to the unit. Besides depression, Johnny has anorexia nervosa – a condition that is somewhat unusual in a male. (Anorexia nervosa is a syndrome marked by severe and prolonged inability to eat with marked weight loss, loss of normal menstrual flow in females, impotence in males and other symptoms resulting from emotional conflicts and biological changes.) During Johnny's recent stay, the staff has been able to work with him successfully enough that he has not had to be fed through a tube in his nose.

Johnny has a great deal of difficulty expressing himself to his family.

"They never know I'm mad, I don't tell them – I just don't eat!"

However, he still has a long way to go. Johnny has a great deal of difficulty expressing himself to his family.

"They never know I'm mad," he says. "I don't tell them – I just don't eat!"

Besides gaining weight, Johnny's therapeutic goals include being honest with himself and his peers, opening up with the staff and expressing his opinions, trying to please himself more than others and practicing these new accomplishments when he goes home.

Emslie says that the short-term stays – usually from a few weeks to two months – are part of the new trend toward short-term hospitalizations in general. Until the psychiatrist took over the unit a little more than a year ago, it had been providing mostly long-term care.

Wiggins, who was in charge of the Children's unit for many years and still supervises its program as a part of his departmental duties, says the main changes in philosophy are in keeping with the mission of the hospital as an acute care facility. It is also in tune with the general trends in health care. Psychiatric stays have been cut because of the increased ability to treat people with drugs and referrals to outpatient care that is now more available. In addition, the high cost of medical care, discrimination against psychiatric care by many insurance companies and the 30-day limit on psychiatric hospitalizations under Medicare have been big factors in limiting hospital stays.

Emslie says he believes the ideal approach is to spend a month diagnosing the problems, working out an individual treatment program for each child and observing his or her progress.

"At the end of that month, if I could keep the patient for an additional two months, could I get him or her to change or would long-term residential treatment still be needed? The best kind of kids to work with are those about whom you get a sense of movement, a sense of change going on in them."

Eleven-and-a-half-year-old Carla was brought in by her family for evaluation recently. Looking at least 15, the girl entered the unit sporting a bleached blonde punk-rock haircut, tight jeans and a full makeup job.

Carla had been running away from home, "hitching" across the state with older friends and staying gone for a couple of weeks at a time. She is sexually active, and, her parents say, has been involved in physical fights with older girls over her boyfriend. Once there was blood all over the room after one of these fights, her mother reported. Because

Carla's family knew of the inpatient program, they brought her in for an evaluation with Emslie.

As soon as a staff member replaced a missing button on Carla's low-cut blouse with a safety pin, she and her parents were interviewed together by Janet Devaney, clinical nurse supervisor. Then Dr. Art Mirzatuny, fellow in child psychiatry on the unit, talked with Carla and gave her a physical examination.

The next step was a meeting of social worker Margery Steindler and Devaney with the parents to acquaint them with the program that includes individual, group and family therapy in the special environment of the unit. In addition, individual staff meetings are held around each patient. The parents also learned that all children and teenagers attend regular school classes weekday mornings and afternoons. They also have physical activities, arts and crafts classes, field trips and entertainment like going to the movies or bowling – all part of a total therapeutic approach to emotional disorders.

"The best kind of kids to work with are those about whom you get a sense of movement, a sense of change going on in them."

After meeting with the head nurse and the social worker, the parents and child sat down with the whole therapeutic team to discuss the therapeutic program and ask questions. The importance of family involvement in the whole treatment program was stressed again at this time.

The family was encouraged to think about its decision and call back in a day or so. If the decision was for admission, an appointment would be made.

On a child's day of admission, staff members meet with the parents and introduce the child to unit personnel, his or her roommates, teachers and classmates.

It is the morning of Carla's first full day in the unit. She is already involved in the therapeutic program and is becoming a part of the group. The kids get up at 7:30, straighten their rooms and dress before breakfast. Carla has already discussed what her problems are and why she is here with her peers. They, in turn, have told her about themselves and why they are in the hospital program.

Twice a week she will meet with staff members and patients in a community meeting to talk about problems in getting along together and how to solve them in addition to participating in daily small group meetings. She will also have individual psychotherapy with her psychiatrist, group therapy

with the other kids and therapy sessions with her family.

A complete physical examination by one of the physicians is given to all patients in addition to the preliminary nurse's exam. Entering patients are also given a battery of IQ and other psychological tests by Dr. Bettie Hardy, UTHSCD psychologist, who also functions as psychotherapist. In addition, any suspicion of physical abnormalities are checked out by EEGs, EKGs and other laboratory tests, and medical consultants may be called into the case.

"One of the outstanding features of the Children's unit," says Waller, "is the fact that some of the finest consultants in the country are available right here in the hospital and through the medical school. I know of nowhere else in the country where this kind of

expertise is so instantly available for pediatric psychiatric patients. This, along with the fact that complicated medical care can continue for patients in the psychiatric unit, is our greatest strength."

Dr. Kenneth Altshuler, chairman of the Department of Psychiatry, agrees that this is, indeed, a "model program."

"Nowhere else in the state and at very few hospitals in the country are there psychiatric units capable of treating patients with severe disease-related emotional problems in a unit with other young patients.

"And we are fortunate to have staff like Graham Emslie from Rochester and Stanford and Dave Waller from Johns Hopkins and Harvard."

Both Waller and Wiggins are board certified in pediatrics as well as psychiatry, and Emslie did some of his training in England under the National Health Services.

Another valuable staff member is Pattie Westerlage, educational coordinator for the Dallas Independent School District curriculum and supervisor of the support child-care workers. "Mrs. West," as she is called by the children, holds a degree in special education and has been working in the unit for 12 years. Besides acting as "school principal," Westerlage is an important part of the therapy team, working with the young people in setting their own personal goals and fulfilling them. This working toward individual goals is an important part of the program. The patients are evaluated by staff toward this end, and privileges are granted on a point system. In order to reach Level IV, the level at which a patient is allowed field trips and fun outings, behavior has to be cooperative and attitude show that the patient is striving in areas of behavior that need more improvement. Because five-year-old Laura is too young to deal with points and charts needed to reach Level IV, she has a special chart with stars and stickers where she can see her accomplishments.

Besides restriction of privileges, the "quiet" room is used for discipline. Patients who are "acting out," upsetting themselves and disturbing others, are sent to the "quiet" room, a place where they can calm down without hurting themselves.

Eight-year-old Don, who has trouble with impulse control, is a frequent visitor. Don's family sent him to the Children's unit for evaluation because they could not control his behavior. He was stealing, running away and setting fires. Testing showed that he had a low level of intelligence and possible neurological difficulties. Don also had a great deal of difficulty getting along with other children and was always fighting. At the end of his stay, it was determined that he needed full-time residential care, and he was transferred to Terrell.

Restrictions are used frequently with 13-year-old Ryan, who has been in and out of special psychiatric programs and seen a dozen psychiatrists over about that number of years. Although Ryan does not test out with as high an IQ as his upper-middle-class family expects of him, in some ways, such as mechnical aptitude, he is almost brilliant. In fact, psychiatric nurse Devaney says that there is no way the lock on the unit door could keep Ryan in: he can pick any kind of lock in a minute. It is thought that the patient's hyperactivity could have interfered with his concentration and thus his learning in his early school years, so that he got behind. Because of his hyperactivity and poor impulse control, Ryan needs a lot of structure and discipline. Going home is not an option for this patient because of the conflict between the young man and his parents. Perhaps a highly structured boarding school and later life in the military will help Ryan function better.

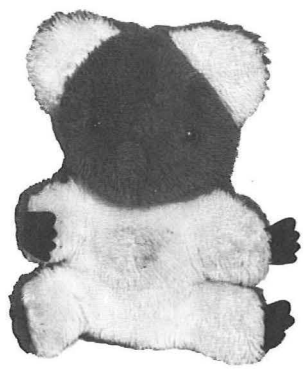
"I don't trust my parents, and they don't trust me."

Since treatment plans are individual, each patient works with the therapists in pursuing individual goals and working to alleviate his or her emotional problems. Learning some basic trust in people is a goal of Shelly's. This patient says openly, "I don't trust my parents, and they don't trust me." Running away from home is one of Shelly's behavior problems, as it is with many of the patients referred for evaluation and treatment.

Staff therapists say Shelly has trouble perceiving reality in the behavior of people around her, and thus believes that her family is "always blaming me, picking on me." Also, the teenager refuses to believe she is depressed. She seeks control and direction in her life by being domineering and overbearing with her peers. Her goals include minding her own business, working on her own problems rather than those of others, not intimidating her peers and talking about her feelings with her family.

It's not always easy to know, or even find out, exactly what the basis of an emotional problem is. And many times the problem is so complicated that all the answers are never sorted out.

"Too often we don't know the cause – although we certainly try our best to



find out – but we can diminish the disability," says Emslie.

This was the case with Janet, a young girl with cyclic vomiting to the point of dehydration. Janet had an hiatal hernia, but whether the hernia was causing the vomiting or just making it easier couldn't be determined. However, life in the therapeutic environment was a major factor in teaching the girl to control the vomiting so she could live a more normal life.

Neurological and metabolic problems are often among the most elusive. Warren, for example, is having an extensive metabolic workup.

Neurological and metabolic problems are often among the most elusive.

And with Laura, the only kindergartener in the unit, neurological testing, as well as metabolic, was done to determine if there were physical complications involved. The child had experienced early abuse and had not had a mother during her formative years.

Laura and her brother were brought to a local child guidance clinic by their new stepmother. The clinic referred Laura to the Children's psychiatric unit.

"When the stepmother first moved in, the children were just like little animals, scurrying from the room and hiding whenever they saw her. They were really lucky the woman cared enough to want to help."

An engaging child with big blue eyes, Laura has learned how to get attention from adults now. But she has no sense of bonding to one special person, a goal the therapists are working toward with her. Since each patient has a "primary person" on both the day and evening shifts, personnel are working toward seeing that Laura, who charms one and all, goes to her special person to satisfy her physical and attention needs. In this way they are trying to teach her to establish the kind of relationship most children learn as infants or toddlers.

Other types of cases seen on the unit include hysterical paralysis and drug-induced psychosis. (A psychosis is a major mental disorder of organic or emotional origin in which the individual's ability to think, respond emotionally, remember, communicate, interpret reality and behave appropriately is sufficiently impaired so as to interfere grossly with his capacity to meet the demands of life.) The latter involved 13-year-old Mike, a leukemia patient transferred from intensive care in the hospital. The strong steroids involved in Mike's chemotherapy caused the young man to think he heard voices telling him to curse at and spit upon people. As soon as his condition was stabilized, Mike was transferred to the psychiatric unit, taken off the leukemia drugs, given anti-psychotics and encouraged to participate in the therapeutic program with the other patients. The change was remarkable, and soon Mike was allowed to return home with his parents.

Emslie, however, does not consider a child "cured" or treatment over at the end of the hospital stay. He believes that the staff is responsible for working out and recommending a continuing program of therapy for each patient or patient and family. Referrals may be made to the UTHSCD child and adolescent outpatient program or a private therapist. A staff member may continue seeing the child and/or family on a continuing outpatient basis, or recommendations for special schools, therapeutic programs, such as the one sponsored by the Salesmanship Club, or long-term care at either a state or private hospital may be made.

Sometimes the victories won in the unit are small. Sometimes they're large. And sometimes the battle is lost.

Sometimes the victories won in the unit are small. Sometimes they're large. And sometimes the battle is lost.

How do team members keep from getting discouraged while working with these children?

"I've worked in this field 11 years now," says Devaney, "and over the years I've gotten such pleasure seeing kids gain their self-esteem. We also get rewards when we see parents bringing kids back to visit and hear that they're having girlfriends, now have friends to call on the phone. Some have grown up and come back to their 'home-away-from-home' on their own. One former patient is an evangelist who's building a church, another's a construction worker, one's a naval officer stationed abroad. Their experiences here played a big part in making them what they are today. I think about these successes." ♦

Editor's note: The names of the patients in this story were changed to ensure privacy.

Little boy blue

When does a child need psychiatric help?

How can a parent – or other concerned adult close to a child – tell when the child's behavior is appropriate for his or her age or when it is a signal that something is wrong?

There is no magic answer to the question of whether a child or young person needs a psychiatric evaluation, says Dr. Kenneth Wiggins, professor of Psychiatry and chief of the Child and Adolescent Division. However, there are guidelines that can be used in deciding whether a professional opinion may be helpful.

First, the adult needs to be familiar with the different stages of physical and emotional development. A good book that might provide helpful insights is *How to Parent* by Dr. Fitzhugh Dodson, published by New American Library. The paperback is $2.95. For other books on child and adolescent growth and development aimed at a lay audience, parents might consult their pediatrician, adolescent specialist or family physician.

After checking out the behavior or behaviors in question, parents might consider:

♦ How frequently does the questionable behavior occur? Was the troublesome incident an isolated example, or is there the beginning of a pattern of behavior? It's not unusual, Wiggins said, for a young child, especially a boy, to set a fire. But if the behavior continues, there is cause for concern. In the same way, little boys may dress up in clothing belonging to a mother or sister, but if the game is repeated over and over, it may signal a desire for dressing in girls' clothing rather than innocent play.

♦ How many other causes are there? If making poor grades at school is the only problem, there may well be no concern psychologically. But if he or she is making poor grades, having trouble getting along with others and rebelling against the parents, that is a different matter.

♦ How generally happy and satisfied is the child? Some children may be doing poorly in school, but it doesn't bother them and the rest of their lives are going well. Also, some children essentially enjoy being alone and spending lots of time on their hobbies. Having a lot of social contacts doesn't seem important to them. However, when a child seems to feel guilty, anxious, aggressive or angry about anything in his or her life, that is a reason for parental concern.

♦ What price (or consequence) is the child paying for the behavior? If the child is skipping school, is he or she slipping behind? If a student misses a lot of classes, then it's hard to catch up, and when one is behind, it makes "skipping" even more attractive. Also, while some children can fight with their friends and forget it the next day, others seem to invite rejection or ostracism by their behavior.

The best rule, Wiggins stressed, is that if the parent feels uncomfortable about something that is happening with the child, a psychiatric evaluation should be sought.

"When a child tells us over and over his arm hurts, we care how the child feels. So we have a physician take a look at the arm. It's no different when we're talking about a psychiatric problem."

Ann Harrell

By Jessica Courtney

Games patients play

Physicians employ the technology of the video arcade in a real life battle against Parkinson's disease and multiple sclerosis

by Susan Rutherford

The fury of the video game is linked to sprained thumbs and sore shoulders as belligerent players clash with fictitious enemies. Winning players are in explicit control over their own reflexes.

Now an adapted version of the video game, charged with checking nerve reflexes and muscle strength, is proving medically valuable. The enemies here are real – multiple sclerosis, Parkinson's disease, myasthenia gravis. Battles against these and other neuromuscular diseases are also real. When disease is the victor, the toll is taken in neuromuscular or sensory deterioration. Interplay between the brain and body can be blocked until initiating a movement becomes difficult, movements once started are slow and ending a movement is awkward.

Neurologists at The University of Texas Health Science Center at Dallas are using video imagery, memory games and other assorted imaginative gadgetry to measure speed, strength and coordination in victims of neuromuscular disease. The idea is to measure disease progression and effectiveness of treatment.

A mini-computer ticks away with a patient's record throughout a battery of game-like tests, counting individual scores and storing them on floppy discs. As a patient is tested month after month, the computer gathers the facts on the patient's condition. "These quantitative measurements are extremely objective – uninfluenced by the hopes of the patient or by the research bias of the neuroscientist," says neurologist Dr. Malcolm Stewart, who along with neurologist Dr. Richard Tindall, has collaborated extensively with the testing system's designer Dr. George Kondraske.

In patients with chronic neuromuscular disease, the computer can tell if patients are 50 milliseconds slower this year than last. Physicians are using the system to fine-tune drug therapy in accordance with a patient's test performance. And surgeons are asking to use the system to measure subtle rehabilitative changes in a patient following surgery.

Patients being tested are asked to move to a number of stations along a row of machine-laden tables. Not all their tasks make use of the video equipment. Near the row of tables is a platform for measuring balance and a chair with motor-driven leg attachments to determine leg muscle stiffness as the patient relaxes.

One test involving the video screen is a random pursuit tracking "game." Holding a control stick, the patient works to keep an "X" on the screen inside a rectangle that is moving fast enough to challenge normal subjects but slow enough to keep patients from giving up. Throughout this test of hand-eye coordination, the computer calculates an error score.

In front of the console is the square platform for measuring body sway and coordination. Standing unassisted proves difficult for many patients lacking neuromuscular control. The degree of imbalance – in right, left, fore or aft directions – is measured by the computer as the patient's weight shifts off the body's center of gravity.

Hand tremor is measured with the arm extended and the hand held inside a loop containing an electric field. Here the computer can detect and quantify movement variations along horizontal and vertical axes.

One middle-aged female patient, walking with a cane into the test laboratory described her coordination problems. Calling her multiple sclerosis a "nit-picky disease," she says it blurs her vision, numbs her arms and feet and makes her sway back and forth when standing unassisted. A baffling disorder, MS comes and goes.

Watching her at the testing console, the technician can see that her left side is much weaker than her right, especially when asked to tap a metal plate with her finger as fast as possible within a 20-second period. Her tapping barely lasted the entire 20 seconds. When asked to hold each of her hands in the electric field to check for tremor, her left hand sank during the 20-second test period.

MS affects the creamy, white substance called myelin, which covers all body nerves and makes for a fast conduction of nerve impulses within the central nervous system. An immunological-based process attacks the myelin and destroys it. In its place scar tissue, or sclerotic plaque, forms. In an occasional patient with an acute form of the disease, MS can lead to total paralysis. The patient's relapsing form of the disease gives her body time between recurrences to remyelinate, therefore repairing itself. But the longer her symptoms persist, the less chance for repair, according to Tindall. Over time, her disease makes for permanent disability.

A local band player first noticed his Parkinson's disease when his left foot refused to keep time with the music. His next clue was that his left arm wouldn't swing like his right as he walked. Four years later he found he had Parkinson's. The musician's test results reflect his unilateral disease. Slowness, weakness and tremor have all been confined to the left side. Now at 55, he is retired and gets "the shakes" only when he forgets his medicine.

Like multiple sclerosis, Parkinson's comes in varieties from mild to severe. Unpredictability is also the rule, but usually it follows a degenerative course. Those in the advanced stages are described by Stewart as "people trapped within themselves." Typically, the early signs are tremor in a hand or foot, muscle stiffness, slowness of movement, a stooping posture, impaired balance and decreased voice volume.

Parkinson's is caused by insufficient quantities of the chemical dopamine in the part of the brain responsible for motor control. Victims may live 20 years or more with medication to fight back the symptoms. But the disease itself still progresses. Rarely the cause of death, parkinsonism weakens patients until they become susceptible to other diseases.

At present, there are no biochemical abnormalities that can be measured to clearly correlate with clinical symptoms for these and other neuromuscular diseases. So typically, neurologists have relied on their own skilled observation to assess a patient's progress.

Kondraske's new quantitative system contains instrumented tests patterned after those in the classical office exam. The system is particularly useful in measuring disease progress after the initial diagnosis has been made, says Kondraske. It replaces the safety pin used to detect pain and pressure sensations, the cotton swab measuring light touch and the hammer for reflexes. It also takes the place of the "finger to nose" test in which the patient moves an index finger from the doctor's finger held at a distance to his or her own nose.

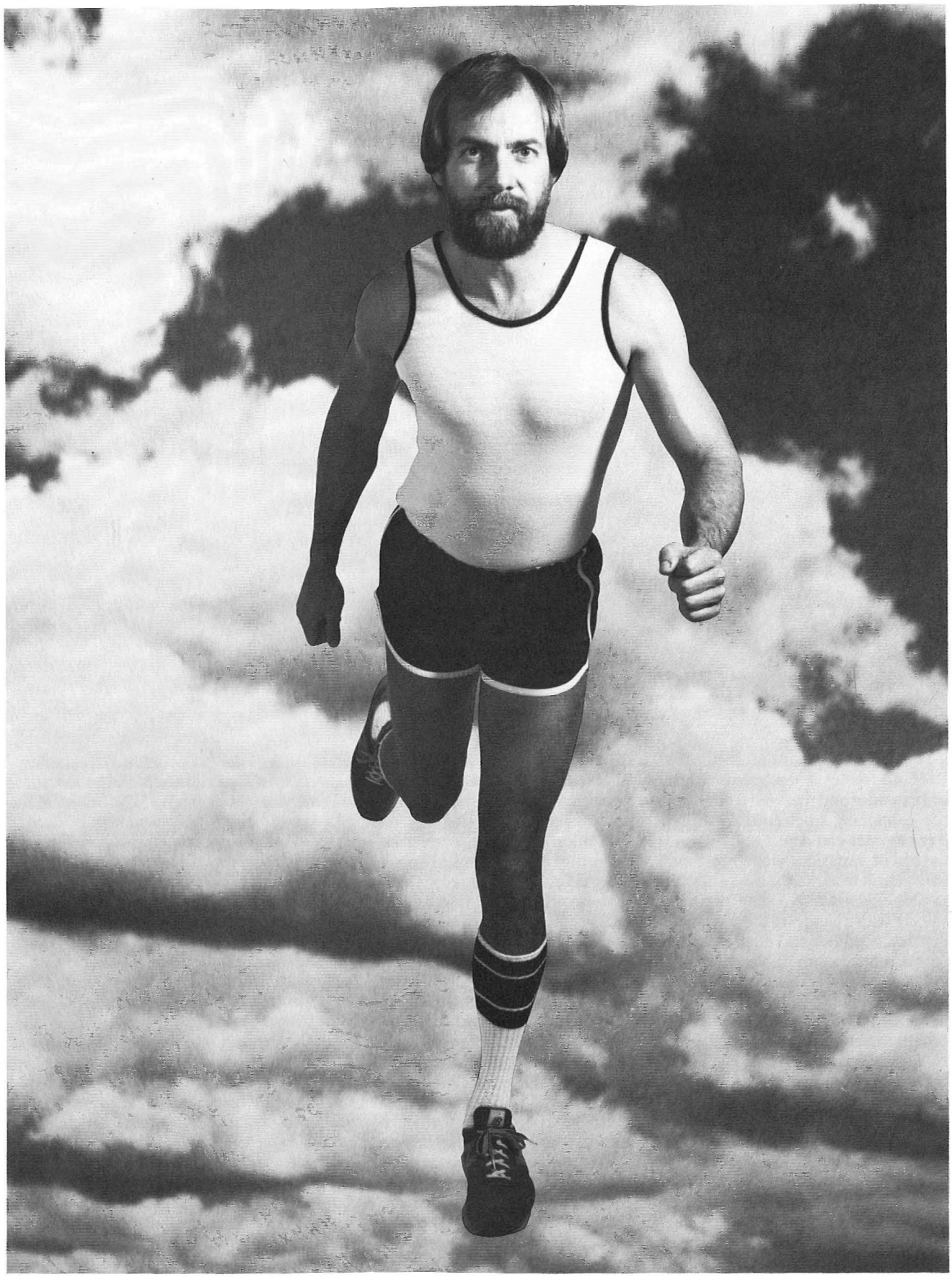
"They say you have to have a number before you can call it science," says Tindall. "Now we have a reliable, quantitative system that can help the clinical neurologist become more objective."

Kondraske relates the brain to an electronic communications system. "We are asking, 'How much information can the patient's nervous system handle?' Often we relate a diminished response by a patient to a diminished channel capacity. In a television set, for example, too much information for the available channel capacity results in a distorted picture. The same idea holds true with the nervous system.

"Parkinson's patients may know what they want their feet and legs to do, but when asked to repeatedly tap on a target sensor with their foot to the left and then tap another target to the right, they begin a labored quivering motion. One can attribute this either to decreased channel capacity or increased noise in the system."

Kondraske says that requests have been coming in from researchers studying a variety of disorders to use the system for drug trials and to measure disease progression. "The beauty of the system is that it's expandable," says Kondraske. Under the supervision of his dissertation sponsor, Dr. Alfred Potvin at The University of Texas at Arlington, and with advice from neurologist Dr. Wallace W. Tourtellotte at Wadsworth Veterans Administration Medical Center, Los Angeles, Kondraske has advanced the "state of the art" in neurologic testing. With a Ph.D. in biomedical engineering, he has a joint faculty appointment in the Department of Neurology here and in Electrical Engineering at UTA.

The machine complex now being used and perfected here is scheduled for shipment in December to the Wadsworth VA and UCLA, Department of Neurology. Plans are being made for up to three identical systems to be constructed for research by our faculty. ♦



DIMENSIONS OF DOPAMINE

A computer plots maps of the brain showing the distribution of this neurotransmitter vital to physical and mental health

When you dance, you're happy, and when you're happy, you dance.

In the "runner's high," movement and emotion are intertwined.

When your team wins the big game, what do you do? You grin, jump up, yell and hug somebody. Movement and emotion.

Sprinkled in generous amounts in both right and left sides of the brain are dopamine-containing cells. When stimulated, these nerve cells spew dopamine into the brain regions affecting movement and emotion.

The basal ganglia (regulating movement) are located next to the emotion region (limbic system), so it's possible the two areas are easily activated jointly, according to Dr. Dwight German, associate professor of Physiology and Psychiatry at The University of Texas Health Science Center at Dallas.

Using three-dimensional computer reconstructions, German and his colleagues, Drs. Don Woodward, Dan Schlusselberg, Wade Smith and Brad Culter, are mapping information that may ultimately show relationships between dopamine cell distribution and the behavioral changes seen in aging and disease.

A computer counts dopamine cells from sections of human brain and plots the position of each cell. When all dopamine cells within a brain region have been charted, one section at a time, the sections are displayed on a screen together in serial order to project a three-dimensional image. This enables the researchers to visualize and analyze changes occuring in dopamine cell distributions as a result of age and disease.

As people get older, they often develop a shuffling gait and emotional changes, probably related to depletions in the dopamine supply in particular brain regions, says German. Age causes a profound decrease in dopamine cell numbers. From ages 20 to 80 the number drops an estimated 50 percent – from 400,000 to 200,000 cells.

Parkinson's disease, sometimes called a "model for aging," is a progressive degeneration of dopamine cells so that one's dopamine supply typically runs out prematurely. Here the loss of dopamine cells may occur at a similar rate to normal persons. However, patients with Parkinson's may have inherited a gene giving them too few dopamine cells early in life.

Scientists are aware that too few dopamine cells create Parkinson's disease while too many may cause schizophrenia. Treatment for these two disorders is often based on moderating the dopamine supply.

Parkinson's symptoms, such as tremor, movement difficulty and muscle rigidity, are treated by giving drugs that enhance dopamine levels, such as the drug L-dopa. These drugs, when given in high doses, can produce schizophrenic side effects.

Dopamine in the brain is related to movement initiation, says German. That is, knowing how much push to give a movement to avoid lunging forward or jerking – the force that pushes movement out. Parkinson's patients have trouble initiating and terminating movement. The marathon runner, on the other hand, is able to rapidly push out movements – smooth repetitive movements – at a fast rate.

A dopamine excess may cause emotions and thought processes to become disturbed, creating schizophrenia. Schizophrenic patients may speak of someone on another planet who is inserting ideas into their heads. Or they may say their own ideas are being stolen by some alien being. Patients may hear imaginary voices conversing and become preoccupied with listening to what is being said so that they lose touch with reality. Dopamine suppressant drugs are effective as anti-schizophrenic medications. These drugs often stop the auditory hallucinations and delusions and in many patients restore them to a more normal life.

When a schizophrenic patient is over-medicated with a dopamine suppressant, the schizophrenia may be controlled, but Parkinson's symptoms often develop.

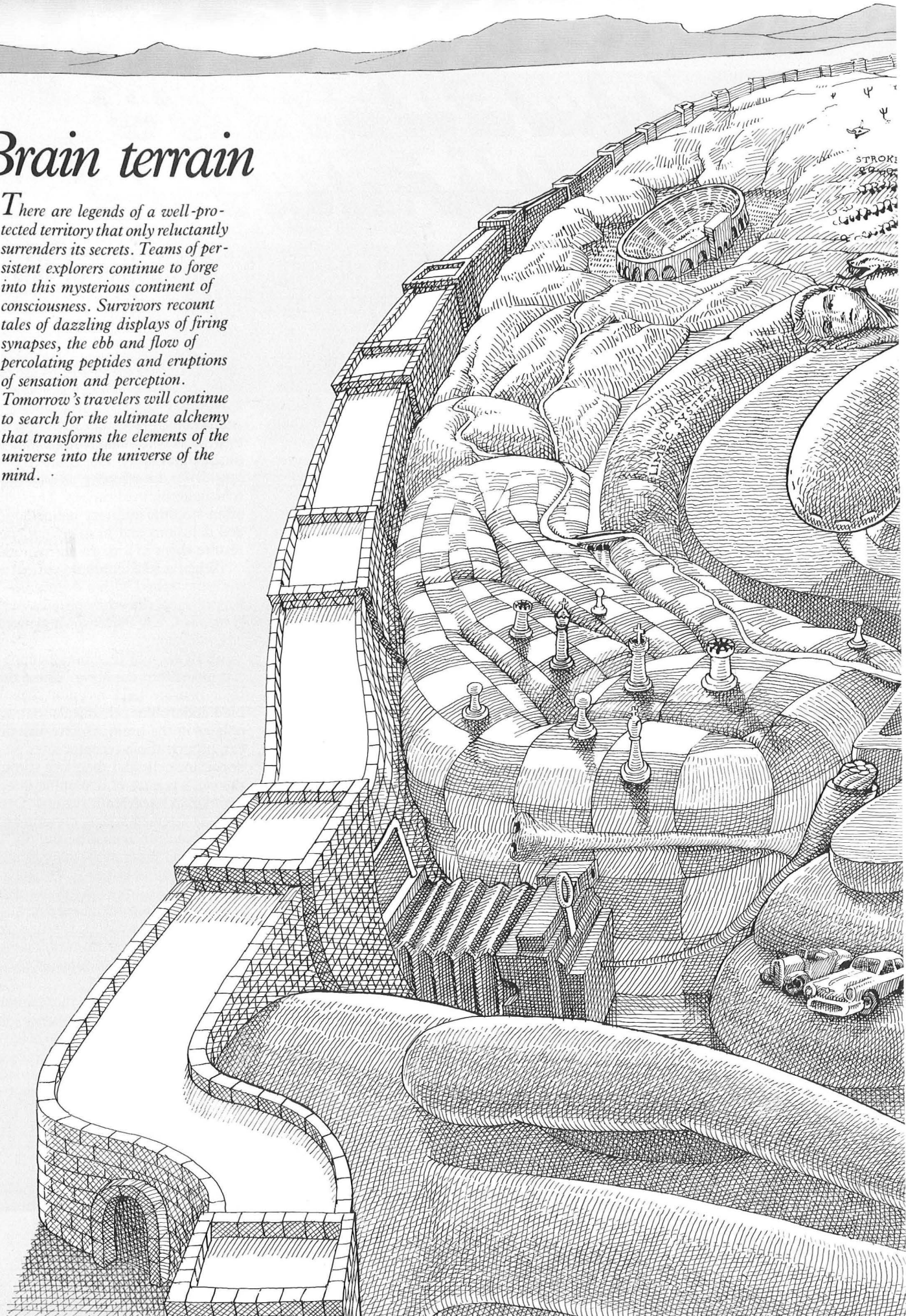
Activation of certain dopamine systems causes euphoria. These dopamine neurons have receptor sites that bind endorphins, chemicals that act as opiates in the brain. Opiate-like drugs can occupy these receptor sites on dopamine cells and therefore stimulate the cell's release of dopamine into emotion-related brain regions. Drugs such as amphetamines, cocaine and morphine spur dopamine activity, bringing on pleasurable sensations. Rats will readily learn to press a lever to inject cocaine into their bloodstream. When cocaine in the blood reaches a certain level, they stop. If you destroy the dopamine cells in the limbic regions, the rats won't self-administer cocaine anymore.

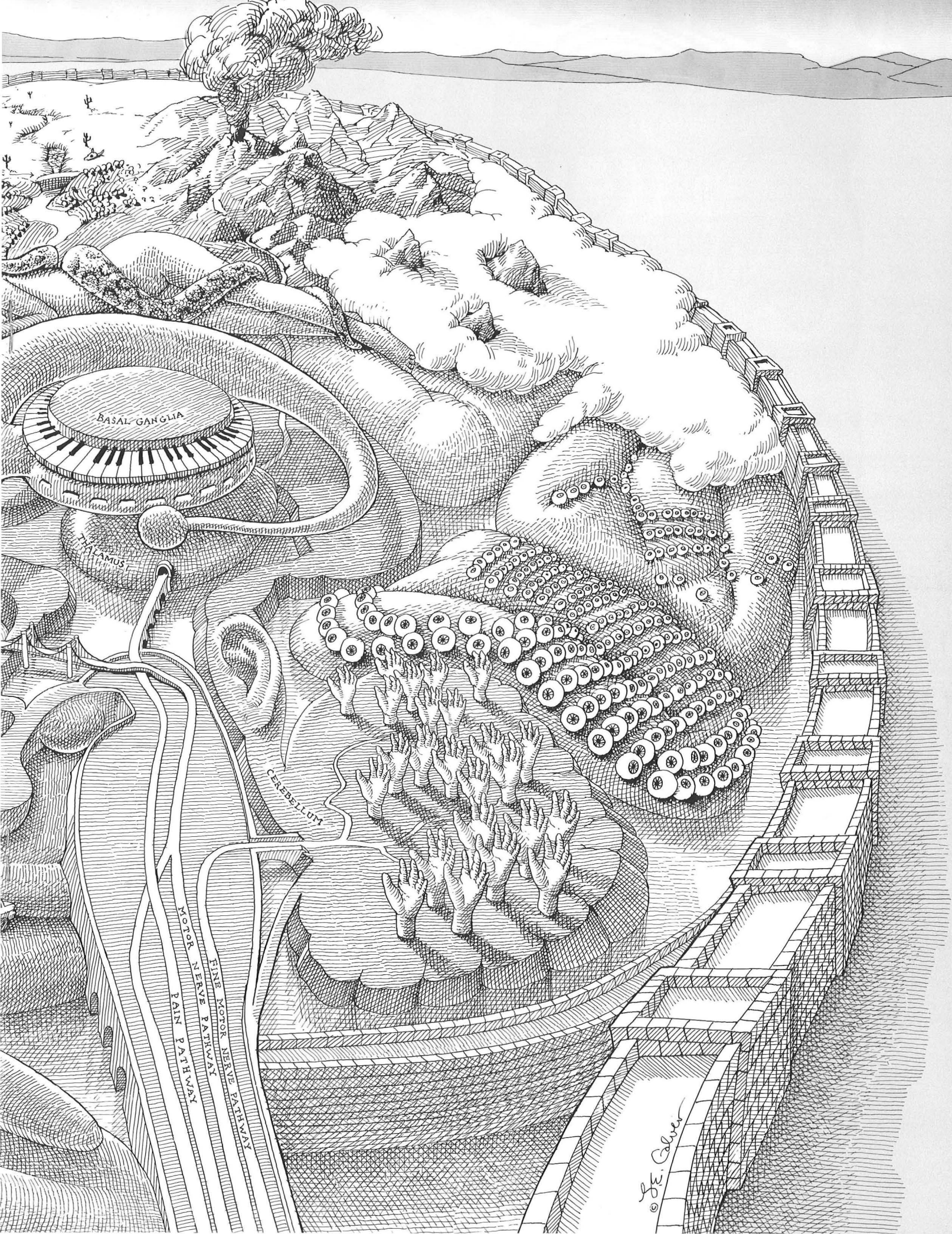
German stresses that the technology is still developing for investigating how the brain's anatomy relates to behavior. But the use of computer graphics as a technique for recording dopamine cell distribution opens doors for new answers on aging and such diseases as Parkinson's and schizophrenia.

Susan Rutherford

Brain terrain

There are legends of a well-protected territory that only reluctantly surrenders its secrets. Teams of persistent explorers continue to forge into this mysterious continent of consciousness. Survivors recount tales of dazzling displays of firing synapses, the ebb and flow of percolating peptides and eruptions of sensation and perception. Tomorrow's travelers will continue to search for the ultimate alchemy that transforms the elements of the universe into the universe of the mind.

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FINE MOTOR NERVE PATHWAY
PAIN PATHWAY
©

The gene game ~ inherited behavior

by Bob Fenley

A mockingbird swoops recklessly down on a cat... a fish changes pigmentation of its scales to display aggression... a blind and deaf child traces a joke in Braille and laughs... a roving male lion invades an unrelated pride and destroys its cubs.

Increasingly, scientists are compiling evidence that there is much of behavior that simply could not be learned– that it is built into the individual by an elaborate genetic code. In fact, it's almost as if the brain calls on a variety of "game cartridges" like a home video machine in expressing personality or temperament.

"There is a genetically determined 'hard wiring' of the nervous system," says Dr. Roger Rosenberg, chairman of the Department of Neurology at The University of Texas Health Science Center at Dallas and co-discoverer of the genetically based "Joseph family" disease. ("Hard wiring" is a popular term used in describing a computer's built-in memory.)

Citing the work of several scientists, including Nobel laureates Konrad Lorenz and Karl von Frisch, Rosenberg explained these ideas have grown into a new field called "neuroethology."

"What they have provided is a body of knowledge that says there is a genetic, non-learned, innate basis of behavior that animals express as aggression, territoriality, jealousy– the temperament of an animal," he added.

"You can see it in teleost vertebrate fish in which the fish will signal temperament by the pigmentation pattern on its scales, which again is a pattern of aggression, of planning to attack, or in the female that she is about to spawn.

The elaborate behavior of the male bower bird in building structures in its courting ritual or the Galapagos goose, which performs an elaborate mating dance over a period of hours, or the Grey Leg goose, which does an egg-rolling ritual in building a nest– all indicate behavior that is not learned but genetically programmed into the individual, says the Dallas neurologist.

As the most highly developed animal, the human displays behavior that is more complex but that well may have a basis in genetic expression.

San Antonio scientist Kenneth Blum, chief of the Division of Drug and Alcohol Abuse at The UT Health Science Center at San Antonio, believes an inherited deficiency of brain hormones called endorphins may predispose some

individuals to become alcoholics. David Comings at the City of Hope Medical Center, Duarte, Calif., has identified a specific brain protein, Duarte PC-1, which occurs frequently in alcoholics and suicidal persons and may be a mediator or predisposer of such behavior.

There is a strong belief that depression is hereditary. This is reinforced by the discovery that there are abnormal cell-surface markers in those persons with manic-depressive illness.

The question of inheritable tendencies certainly was raised by the recent suicide of Leicester Hemingway who joined his famous brother, Ernest, and father, Dr. Clarence Hemingway, in self-inflicted death.

Although there may never be a definitive answer to this question, there are definite behavioral patterns connected with scores of genetic neurological diseases.

Rosenberg, an authority on this subject, points out that:

"There is strong evidence in humans that a mutation on the X chromosome can result in a striking alteration of behavior. This is evidenced in the Lesch-Nyhan disease which is an X-linked recessive disease where the mother is the carrier and 50 percent of her boys develop the disorder.

"They mutilate themselves. They bite off their lips, and they bite their fingers. They have very high levels of uric acid in their blood and high levels of oxypurines in their brain. The enzyme defect is known–HGPRT is deficient.

"These boys may be of normal intelligence–or moderately retarded at the most.

"They do not want to mutilate themselves. They implore, 'please tie my hands down... please pull my front teeth out.' It's painful. They don't want to perform this kind of behavior, but they have this obsession, this obsessive-compulsive behavior to self-mutilate.

"Obviously, there is a profound alteration of biochemistry of their brain that is under genetic control and underlies a striking change in human behavior."

Perhaps nowhere else is the division between the intellectual and the obsessive so sharply focused.

"There are inbred strains of mice that have a specific temperament as well as level of intelligence. Some strains developed since 1940 have varying degrees of aggressiveness and varying degrees of maze-learning ability.

"You can also show that levels of important neurotransmitters (chemicals that help carry nerve messages)–specifically acetylcholine–are high in the frontal lobes and the temporal lobes of these more gifted animals," said Rosenberg.

"At the human level it is important to look at the development of the child. Irrespective of the race, of the ethnic origin, of the culture, of the geography, the nervous system develops in a programmed, timed manner that is independent of these variables.

"A child begins to follow an object at a month of age, will turn over at about two months of age, will sit at about five months of age, stands at 10 months, starts to walk at about a year, begins to speak in simple words at about eight months, phrases at about 15 months of age, simple sentences by two years, learns to ride a bicycle at five, develops higher intellectual functions between five and 15 years of age.

"What you're looking at is the genetic program for development of the nervous system, which is not learned and which is independent of these variables.

"You do need an environment to enrich this potential. There have been bizarre cases in which a child has been put in darkness and neglected for years. And the development of the nervous system of that child is impaired. So you do need an environmental reinforcement to bring out that genetic potential," explained Rosenberg.

Harvard biologist Stephen Jay Gould has said, "Genes do not make specific bits and pieces of a body; they code for a range of forms under an array of environmental conditions. Moreover, even when a trait has been built and set, environmental intervention may still modify inherited defects."

The genetic program responsible for brain development calls for multiplication of nerve cells in the fetus' first few weeks. This is followed by a sorting out of cell types and this is followed by a migration out from the core area around the neural tube to form the mature structures of the brain like the cerebral cortex, the cerebellum and the basal ganglia.

There now begins formation of "processes" of the cells, referred to as dendrites and axons, leading to synaptic connections, followed by spine formation and formation of multiple small connections. The final "spining" provides the interconnections between neurons in the brain, giving the staggering number of combinations used in the thought process.

"In other words, the genetic code is responsible for the hard-wired diagram that eventually develops," said Rosenberg, "and this is independent of any characteristic of learning, race or geography.

"Very important for human development is the formation of spines on dendrites at the very end of this process. You can have a child that hears and sees and speaks and walks and talks and feels and yet is profoundly mentally retarded. The difference is, while the brain is apparently fully formed, that final, terminal spine formation step has not matured as it should, resulting in retardation.

"This shows that the entire process of the genetic code for brain architecture is necessary to produce truly human behavior."

Graphically demonstrating the built-in genetic behavioral processes is the child who has been blind and deaf since birth, who has never seen anyone laugh, who has never heard laughter, but if you communicate by Braille with this child and tell him something humorous, the child exhibits the expression of laughter, and actually laughs, said Rosenberg.

"The emotions, if you will, are hard wired."

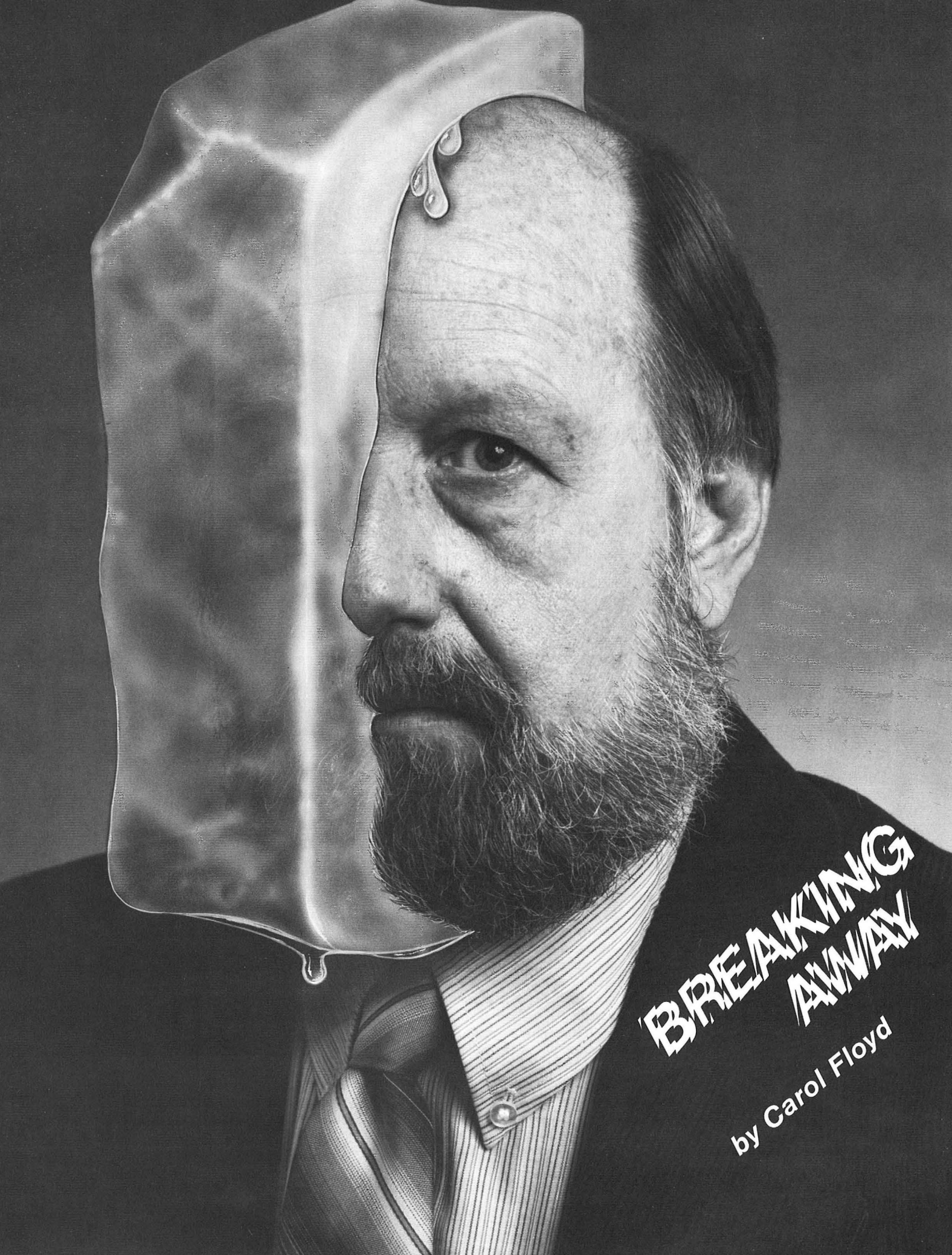
There is a somewhat controversial regime of thought called "sociobiology" that declares there are sets of genes that determine primitive human behavior as it does in animals–behaviors such as hunger, sex, thirst, territoriality and aggression, he explained.

"However, the sociobiologists will say that some concepts such as altruism, fair play, justice, honesty, are also under genetic control as techniques for biological survival."

A parent who saves a child from a burning building, the behavior of a mockingbird in driving a cat away from its nest and even a lion that destroys cubs of another pride–all could be carrying out biological maneuvers to preserve genes closest to the individual.

"Look at the repertory of human behaviors. Irrespective of race or culture, complex behaviors as religious feelings, incest taboos, marriage rituals, group bonding and cleanliness seem to have arisen spontaneously in separated primitive tribes.

"There's something here, I think, that transcends civilization." ♦


BREAKING AWAY
by Carol Floyd

Recovery of stroke victims through rehabilitation requires a team of health professionals

Its disabling nature and the dreaded dependency it may produce make stroke the most feared disease among older Americans. Yet the body's own healing powers combined with refined therapies make recovery and independence possible in many cases.

Most stroke victims who have hemiparesis, partial paralysis on one side of the body (a common occurrence in the majority of strokes), walk again. Arm function returns, but not always hand function. Drooping facial muscles can be controlled. And speech is often restored.

"If you follow patients neurologically for years, the amount of recovery is very significant," says Dr. Elliott D. Ross, associate professor of Neurology and Psychiatry at The University of Texas Health Science Center at Dallas.

These improvements are largely a result of "spontaneous recovery," the body's natural healing mechanism, although therapy may assist in speeding up or maximizing gains. Following the acute injury and subsequent treatment of immediate medical problems, a neurologist or internist may order specialized therapy for a stroke patient. Yet, without intervention, the brain is still capable of significant reparation.

Acute recovery, the reduced swelling of the brain and reduced bleeding, occurs within the first two weeks of the insult. Intermediate recovery in which information is rerouted in the brain to compensate for damaged areas may take up to six months. Long-term recovery is the very gradual return of movements and functions after six months. This pattern represents the optimum recovery process, says Ross, stressing that any patient may plateau along the way and make no further improvements.

"In general, the recovery is related to how well the nervous system can recover from the insult...that is the most potent cause for recovery," Ross explains. "Therapy prevents things from worsening and aids in maximizing neurological recovery. But there is very little therapy can do to retrain the brain when crucial areas have been destroyed.

"Orthopedically designed therapies directed toward return of movement and function of limbs and preservation of joint integration are very beneficial. Neurologically directed treatment aimed at speech and intellectual recovery, however, is much more difficult and uncertain," he continues.

Physicians – usually neurologists and internists – who treat the stroke patient initially, rarely witness the patient's long-term recovery. Progress is monitored instead by a rehabilitation team consisting of a physical therapist, an occupational therapist, a physical medicine and rehabilitation specialist and a counselor, depending on the extent of damage. Because functions are distributed in different areas of the brain – certain areas control motor activity, sensory functions, speech and cognition – the site and extent of the brain injury determines resulting symptoms.

Stroke or cerebrovascular accident (CVA) is the sudden onset of neurological dysfunction that usually results from infarction (death) of brain tissue due to blockage or bursting of blood vessels in the brain. Approximately 50 percent of all strokes are caused by thrombosis, obstruction of blood flow to the brain by a blood clot usually due to atherosclerosis (the build-up of plaque and fat inside the vessels). Sometimes a thrombus may break apart and become an embolus, a clot that moves in blood vessels from one area to another until it blocks a blood vessel; this condition occurs in about 30 percent of stroke victims. Another 20 percent suffer cerebral hemorrhage, the most devastating of strokes with the greatest incidence of death.

"People who have had a thrombus or embolus usually have a better long-term prognosis than those who have had a hemorrhage because the bleeding can affect a great deal more tissue in the brain," says Dr. Demitri George, assistant professor of Physical Medicine and Rehabilitation.

In the bursting variety, a stroke may result from an aneurysm, a sac that forms at the end of arteries with weak walls, that eventually ruptures. Little aneurysms in very small arterioles deep within the brain may burst if one's blood pressure is high enough, resulting in intracerebral hemorrhage.

High blood pressure also causes premature aging of blood vessels, which may lead to atherosclerosis. Eventually the formation of plaque closes off the blood vessel, blocking blood flow through the arteries and causing a stroke. In most atherosclerotic cases the neck vessels are clogged; however, sufficient blood flow through other routes to the brain may prevent a stroke.

Persons who have had heart disease are subject to blood clots in the lining of the heart or along the valves. These clots can break off from the heart and move up to the brain area, obstructing the blood flow. Underlying disorders including hypertension, diabetes and obesity also increase the likelihood of strokes. Since these conditions usually worsen with age, the elderly are most susceptible to strokes and have a poorer chance for recovery than younger people who do not have generalized vascular disease.

"The most potent risk factor for strokes is high blood pressure. If you control a patient's hypertension, you will markedly reduce his risk for strokes," Ross says.

The brain's right hemisphere controls the left side of the body and the left hemisphere regulates the right side of the body. So a lesion to either side's motor center would cause paralysis in the opposite side of the body. A person may be bilaterally affected, but this is rare.

Another rare type of stroke, the most catastrophic of those affecting the motor system, destroys total motor output and movement in all extremities while leaving intact all sensory inputs to the brain. A person affected in this way is capable of processing information, yet is unable to respond in any physical or verbal way. A rarity, striking only about 40 to 50 people in the U.S. each year, this condition is known as the "locked-in syndrome."

The anatomy of the brain is such that the areas, called motor systems, that have to do with movement are connected to the spinal cord, which is connected to muscles that move one's

limbs. Anatomically distinct from motor output, sensory input goes through the ears, eyes and other sensory organs, each through a separate bundle of nerve fibers to the cortex where sight, hearing, smell, taste and touch are perceived.

The locked-in syndrome is caused by a lesion that usually occurs in the basis pontis, the anterior portion of the pons in the brain stem where the vast majority of motor fibers run. It is usually caused by thrombosis of the blood vessels to the basis pontis. The posterior portion, which houses the sensory tracks and reticular activating system (the alerting system of the brain that allows a patient to stay awake), remains uninjured.

The patient can breathe unassisted since the lower brain stem, which provides the automatic mechanism for breathing, is intact. Involuntary movements – the repositioning of legs or arms – are not mediated by the cortex, but by spinal cord neurons and usually occur with a painful stimulus.

The one motor movement the "locked-in" patient can perform voluntarily is eye blinking. Deprived of any other means of communication, the eye blinking becomes a "Morse code" in which a physician can establish the fact that sensory information is entering the patient's brain and being perceived.

It is possible to mistake a locked-in patient for a comatose patient since some comatose patients have their eyes open and appear to be awake (a condition known as comavigil).

"The crucial issue for a physician is not to miss a patient who is locked-in and assume they are comatose and then treat them as if they were comatose, talking in front of them at the bedside and things. Obviously if they are locked-in, they can feel pain so you must nurse them carefully," Ross says. In fact, the level of nursing care makes the difference whether a patient lives or dies in this situation. "They usually die because they don't move their legs or arms so they get ulcers and bedsores. You must feed them through a tube because they can't chew or swallow. You have to watch their respiration. So with the sheer nursing problems, a lot don't make it, yet some stay alive for years and years.

"You would think that if you were given the choice of being alive or dead in that situation, most people would choose to be dead." Yet Ross recalls the story of a woman who was locked-in and through a pattern of eye blinking communicated her feelings and thoughts to her husband and was able to write a book.

"Her point was she would rather be alive," Ross says. "In fact, she was very happy to be alive because she was able to see her children grow up and interact with them, look at television and feel things inside emotionally."

Most stroke patients though are capable of varying degrees of rehabilitation, says George. He notes that about 50 percent can become independent in a home situation, 30 percent are employable and the remaining 20 percent require specialized care outside the home.

The length of recovery time varies from patient to patient although it is not unusual for recovery to take up to a year. Damage caused by lack of oxygen in the center of the lesion is permanent but peripheral damage is often partial and temporary. So initially lost functions may eventually be restored.

Motor impairment may result in flaccid limbs, hypertonia or spasticity. A person may become spastic because the anti-gravity muscles are typically affected. For instance, the arm may be turned up and rotated, unable to swing normally. The leg may be rotated and tipped down, making normal coordination of motions impossible.

To decrease spasticity, which practically all stroke patients have to some degree, George says physicians are renewing old techniques of sensory facilitation – using splinting, positional changes and bracing. Spasticity is brought about by uninhibited spinal reflexes, and by utilizing sensory and motor feedback these reflexes can be inhibited.

As spasticity is reduced, patients can better control their upper extremities in performing daily routines at home or work. Recovery of the limbs nearest the center of the body is greater than recovery of the parts farthest from the body's trunk; this means arm function is typically regained but fine finger movement is not.

Returned use of the lower extremities is more frequent than returned use of the upper extremities because of the way the motor systems are organized in the brain.

While sensory facilitation will not increase voluntary movements, it will improve whatever voluntary movements are there.

This technique is replacing formerly used "destructive procedures" such as medication and surgery to control spasticity. "In the past medication such as Valium was used and that is not an ideal situation for stroke patients because it affects their mental status. Surgical procedures can actually decrease function by destroying nerves or cutting a tendon. The results so far with sensory facilitation are as effective as medication and surgery and don't have the disadvantages," says George.

Once a stroke patient is medically stable, physical therapy is necessary to encourage movement, range of motion and tonal reconditioning.

Sue Smith, instructor of Physical Therapy, says the normal motor skills children learn – rolling over, standing and walking – must often be relearned by patients.

"While therapists use rehabilitative techniques that are similar in sequence

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and mechanics to the normal development of motor skills, it is different from a child who has not previously experienced a full repertoire of motor activities. Since adults have learned these activities before, therapists identify the components that are missing or abnormal in the movement and assist the patient in relearning the components and reintegrating these into function."

What is lost typically is the normal postural reflex mechanism, which gives one a sense of balance. This combined with the sensory dysfunction of being unable to feel in the extremities may lead to balance problems, which, in turn, affect the person's daily functions of eating, dressing and attending to basic needs.

"There are certain reflexes or reactions we call upon to maintain our balance that patients may have lost, so they are very fearful of falling," says Smith. "Lost confidence is a problem for the patient to overcome when working to regain mobility."

Normally, persons receive sensory feedback telling them where their body is – a visual and proprioceptive sense – allowing for normal postural adjustments. Stricken people may not receive this feedback.

"I remember a patient who had his own arm draped across his body and he didn't realize it was his, " she recalls. "It is very difficult to retrain a patient to use a part they can't identify as their own."

A patient may spend weeks in a rehabilitation setting immediately following a stroke. During this time specialists actively work toward reteaching primary skills to increase mobility and foster a sense of independence. Usually stroke patients are taught to walk on their own, sometimes with braces to prevent the foot from dropping down, making wheelchairs unnecessary.

Some patients may lose motivation as a result of their stroke, making rehabilitation difficult. "Motivation is one key to being rehabilitated. As therapists, we motivate patients and we do that by encouraging their progress, showing them the positive results of their efforts," Smith says.

Since the energy expenditure required when someone has normal functioning in only half of his or her body is much greater, patients in therapy tire easily compounding motivation problems and leading to a sense of frustration. Yet paralysis is not the major problem in stroke rehabilitation.

"The biggest thing stroke patients face is abnormalities in their mental status," George says. "Cognitive functions are affected routinely by all kinds of strokes."

Depending on the brain areas destroyed by the stroke, one may suffer language deficits, memory or concentration loss or the inability to make judgments, calculate or conceive of things.

Diagnostic tests and machines are used to pinpoint mental deficiencies. The CT scan – computerized tomography – reveals the area affected and the cause. Standardized therapy including speech therapy and occupational therapy that stresses perceptual training works to improve cognitive function although there is only a limited amount of retraining possible.

Says Ross: "Once a piece of brain tissue goes, there's no replacing it so other parts of the brain have to take over for it. Some people do it very well, and some people don't." Mental recovery is better if the brain damage is small and the person is young or left-handed.

The brain's left hemisphere contains proportional language functions – word choice (lexicon) and order (grammar). Damage to this area may produce "aphasias," the inability to communicate coherently. A patient may be afflicted with receptive aphasia (the inability to understand what is spoken), expressive aphasia (the inability to find the words to say something) or global aphasia (both).

Right hemisphere damage may produce a loss in the emotional components of communication, making speech devoid of musical coloring, animation and emotional tone.

Speech sounds different following a stroke, depending on where the lesion occurred. If the lesion were in the front part of the brain, words would be hard to articulate. If the lesion were in the back part of the brain, words would spill out but would be paraphasic (misused), nonsensical, mispronounced or made up.

If one has a very dominant left hemisphere for spoken language and the stroke destroys it, then there is little room for recovery. But, if dominance is distributed between the two hemispheres, the other hemisphere can take over.

Despite partial mental and physical recovery, most stroke patients cannot work outside the home.

"If you put them to work in job situations where they need to make fine judgments on paper or physically, you may have problems," George explains. "The large majority of stroke patients are unable to return to former employment or employment in general, but that doesn't mean they are invalids. They can do volunteer activities where decision-making is not that important or take over family responsibilities."

A patient may exhibit impulse control problems, inappropriate sexual gestures or emotional insecurities following a stroke, says Dr. Fred Cromes, associate professor of Clinical Physical Medicine and Rehabilitation and chair-

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man of Rehabilitation Psychology. "These behaviors are a result of what happens to the brain more than a result of some drastic personality change."

Counseling of family members increases understanding of the patient's condition and helps guide them in caring for and interacting with the patient.

There is a tendency among some stroke patients to become overly dependent on their spouse or family to do things for them. "If you comply with all their demands, you reward that helpless behavior and they don't learn how to do things for themselves. It's important to pay attention to their progress and reinforce the good things they do. There is a tendency in society to pay attention only to the mistakes," Cromes says.

Marital break-ups as a result of stroke are rare among older stroke patients although definite lifestyle adjustments must be made.

"The more stable a marriage was before the stroke, the more likely it is to be a productive relationship afterward," he says.

Younger people who may be raising children and dependent on their job income face greater family strains.

Regardless of the patient's age, certain determinations must be made by a trained expert before that person returns home. "There are so many questions of competence. Does that person have the sense to remember he or she can't feel heat with one hand, does a person have the capacity to put the ingredients in a recipe, can a person hold his or her kids and move around enough to discipline them? And how will a kid react to a mom or dad who is different?" Cromes says.

Certain modifications in the home such as grab bars around the bathtub and commode, kitchen adjustments, accessible bed heights and others ease the transition from hospital setting or rehabilitation center to the home. Once home, outpatient therapy may be required for fullest recovery and underlying medical problems continue to need treatment to prevent their worsening or stroke recurrence.

Considering the initial devastation following a stroke, it is a wonder ultimate recovery is as great.

"When you see someone come in who is unconscious and with no use of one side of his or her body, and a month later they are walking and conversing, that's remarkable," George says. ♦

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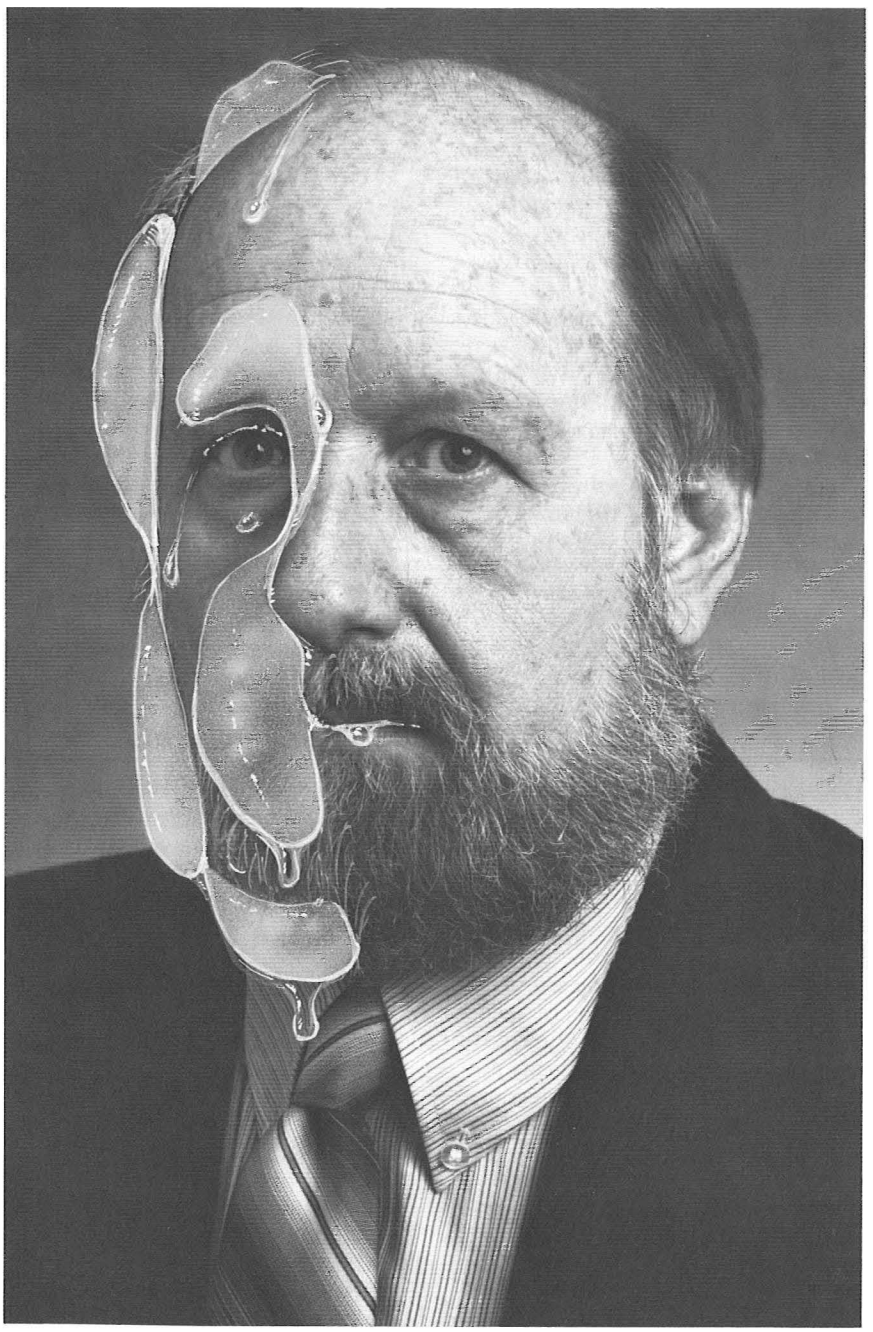


Penetrating the pathways of pain

by Liz Willding

A foreign signal triggers a spark.
The electrical blast travels up one live wire to another, connecting circuits, commanding responses. Snapping and popping in split-second time, the signal evokes a reflex, even before being perceived.
The reflex is defense; the perception is sensation.
Defense plus sensation equals pain.

One of life's basics is pain. Within the thalamus and cortex of the brain signals spark a newborn to cry out in response to a quick clap on the behind, or even the stressful emergence into a foreign environment. In these same regions of the brain an elderly person may know the aching and throbbing of an arthritic joint or an old injury.

Scientists and physicians say they know everything and nothing about pain. They define the pain that comes from injury or internal breakdown as acute and talk with confidence about pathways of nerves within the body and brain that chart its predictable course.

A textbook description of acute pain begins with adverse stimulus to the skin or a deep sensation that is usually due to displacement of tissue within the body.

The stimulus evokes nerve cells or receptors that initiate changes in electrical charges to nerves or muscle fibers. These electrical charges progress through three levels of fibers before reaching the thalamus and then the cortex of the brain.

The first level of fibers, called the dorsal root ganglion, are located at the base of the spinal cord. It is at this site that the message is "read" and, if interpreted as a danger signal, is sent on.

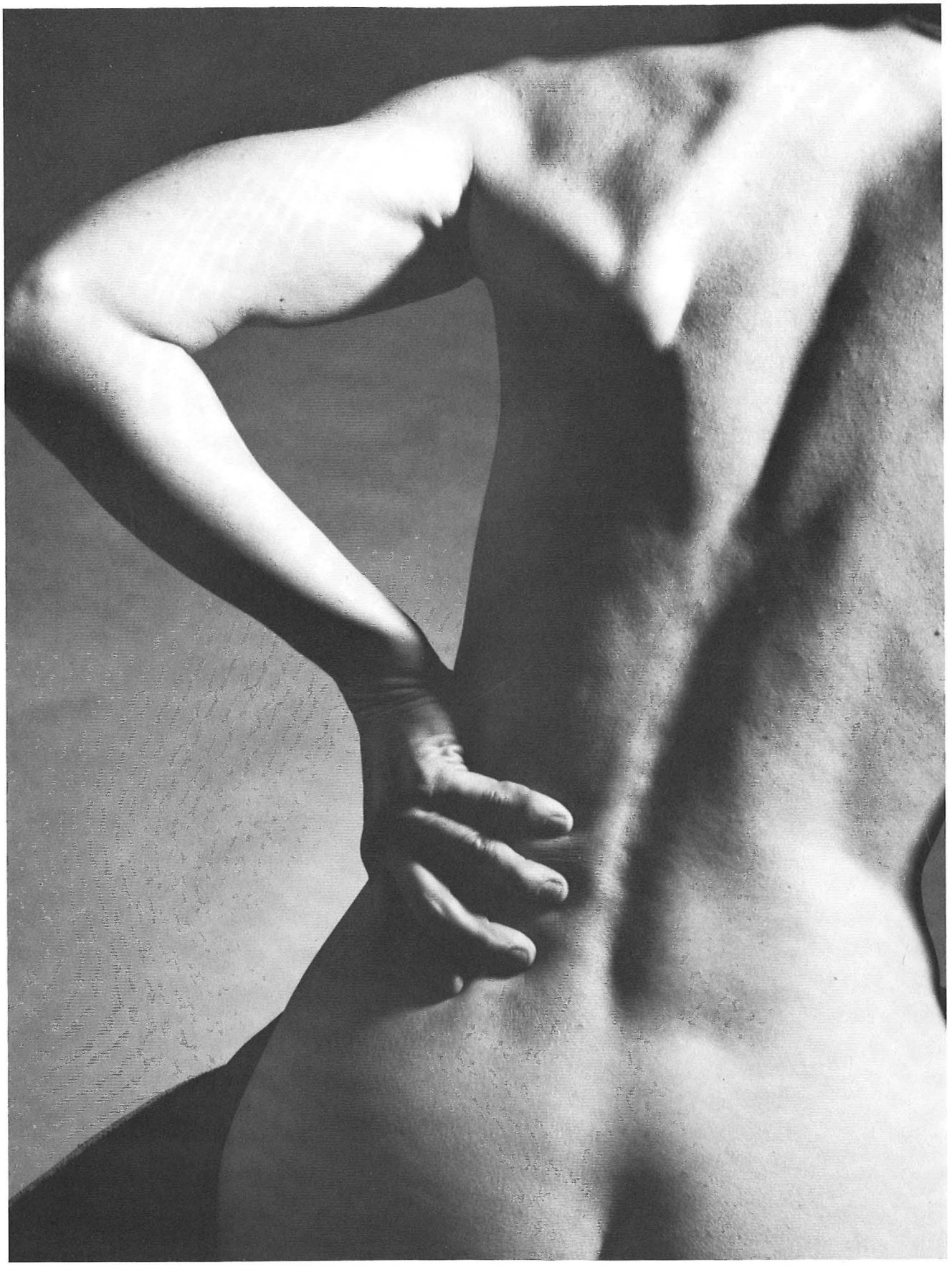
If sent on, the nerve signals next move up the spinal cord to the substantia gelantinosa or second level of fibers. These fibers control a reflex mechanism that signals the body to pull away or "flee" from the dangerous stimulus.

While this mechanism goes into action, signals progress to the third level of fibers or the thalamus in the brain where the pain is actually perceived. From the thalamus the signals complete their journey to the cerebral cortex where the pain is "felt."

By charting these pathways, doctors know that even before pain is perceived in the thalamus or thought about in the cortex, the body is reacting, pulling away from the pain through reflex responses.

There is yet another form of pain that leaves them puzzled. They call it chronic pain because it lingers, usually growing in intensity. Chronic pain defies the laws of neuroanatomy. Some say it lacks meaning. Instead of acting as a mechanism of survival, it acts as a threat to survival.

Chronic pain comes in a variety of forms. It can be a recurrent headache, a nagging backache or a constant aching from an old knee injury. In many cases there is no or minimal medical evidence to attribute it to, other than the com-



plaints of the patients.

A mysterious but very real problem in society, chronic pain has often been passed off as a mental deficiency on the part of the patient. Some surgical techniques have been used to break pain pathways by actually severing nerves. Although these techniques are successful for some cases, the pain often comes back.

At The University of Texas Health Science Center at Dallas researchers are studying a number of links to chronic pain, links that may suggest that the problem is not "all in the mind" but, at least in part, a result of biological deficiencies.

Drs. Manoochehr Khatami, associate professor of Clinical Psychiatry, and Sandy Kiser, associate professor of Psychiatry, are looking at the effects of natural pain-relieving chemicals in the body called endorphins and their response to the mysterious but effective technique of acupuncture in chronic pain patients.

"The patients we are accepting into the study seem to have no medical, surgical or psychological causes for their pain. We give them a battery of tests to confirm that their pain is not linked to a known cause," Khatami explained. Testing includes psychological measures and a relatively new blood test to determine biological depression.

Khatami explained that biological depression is established through the dexamethasone test. "We can determine if a patient's depression and subsequent pain is biological by giving them dexamethasone (chemically related to cortisol) and then measuring the level of cortisol in their blood. If they are not biologically depressed, they will normally suppress the cortisol levels. Those who are biologically depressed cannot suppress the cortisol because there is a disturbance of their hypothalamic-pituitary axis."

If depression is not causing the chronic pain, the next step is to analyze the level of the pain-relieving endorphins. Once baseline blood and spinal fluid levels are established, acupuncture treatment begins. Following the last treatment of acupuncture, blood and spinal fluid samples are taken for post-treatment measurement of endorphin levels.

Khatami explained that his part of the study involves administering the acupuncture to patients and performing the psychological tests. "No one really knows how acupuncture works," Khatami said, "but it does relieve pain."

Of Chinese origin, acupuncture was met with much skepticism when it was first introduced into the western world. It is administered to specific acupuncture pressure sites that are linked to the relief of pain in specific body sites.

"Modern day acupuncture is a little different from the ancient Chinese methods," Khatami explained, "but the principles are the same. Today we use small needles that are connected to a device that delivers small pulses of stimulation. This stimulation to the acupuncture points relieves pain in many cases."

Khatami and Kiser are trying to find out whether the electrical stimulations actually cause an increase of the pain-relieving endorphins in the blood and spinal fluid.

"We have known about the endorphins for some time now," Kiser explained, "but we have been unable to say what their role in chronic pain is. The question has been raised whether an imbalance of these chemicals may be one cause of chronic pain."

"Many things can contribute to chronic pain – stress, depression, social factors. It's a big picture."

Kiser explained that pain-relieving drugs like opium and morphine mimic the effects of these natural substances. "Chemically, the endorphins are peptides," he said. "It is estimated that approximately 20 types of endorphins exist.

"There is controversy over how they work. Some theorize that they appear to block pain as the pain is carried from the peripheral site of injury into the spinal cord. Or at the point of entry to the brain, the message may be interfered with.

"There is also evidence that the pain message may be processed at more elaborate levels. In the limbic system of the brain for instance, there seems to be a large concentration of cells that have endorphin receptors. Endorphin receptors are sites that attract the pain-relieving chemicals.

"The limbic system of the brain is thought to be involved with emotionality so it is speculated that this is why the endorphin/opiate drugs seem to have a soothing, calming effect. Persons who are given opiate drugs generally still feel the pain, but they are not as bothered by it."

Kiser uses a technique he learned at St. Bartholomew's Hospital in London to measure the endorphins. "The problem with measuring endorphins has been that, because there are so many, it has been hard to tell which endorphin is being measured.

"In our current study we are looking at two endorphins, beta-endorphin and met-enkephalin, along with ACTH (a related peptide). The tests or assays that we are using utilize highly specific antiserums, and we are able to tell exactly what we are looking at."

The researchers have established that acupuncture stimulation does appear to elevate beta-endorphin levels in the bloodstream. However, the amount is slight. They postulate that higher levels may be released in the spinal fluid. Tests are currently underway to explore this possibility.

"It is too early to say because we haven't completed all the assays," Kiser says. "We are also wondering if these patients have a lower than normal level of endorphins to begin with, which might be contributing to their pain."

Kiser and Khatami agree that the solution to the problem of chronic pain is very complex. "This is just one area," Khatami said. "Many things can contribute to chronic pain – stress, depression, social factors. It's a big picture.

"We plan to compare the effects of acupuncture and endorphin levels to other pain-relieving techniques like biofeedback to see how much of a placebo effect we are getting."

Although the two doctors approach inquiries on the outcome of their work with caution, they are excited by the success of the acupuncture treatment.

"Sixty to 70 percent of the patients are experiencing pain relief," Khatami said. "It would be very nice," Kiser concedes, "if we could find out that there is a specific abnormality that underlies most of these cases and then devise a way of dealing with it."

The two doctors believe one thing is sure. The pain is real. "It is very rare – less than five percent of the cases – that someone is lying about their pain," Khatami explained. "It is often misunderstood by the medical profession, but it is real and it crosses every discipline of medicine." ♦

DNA probes the chain of command

Scientists can study the development process in brain cells using recombinant DNA

by Ann Williams

Brain cells contain the information that makes us what we are. Brain cells, like every other cell of the body, contain the genetic code in their DNA (deoxyribonucleic acid) to produce every protein that is produced in the body. Every life process that takes place within a cell is mediated by a specific protein. But specific chemical events trigger the production of only the proteins that a cell needs to make – when things go normally.

Cells operate like miniature factories, producing whatever proteins they need to carry out their particular function. The DNA is the computer that contains the instructions for making a particular protein. Tubulin, for example, is a protein involved in cell division and cell structure. When the cell needs tubulin, some unknown trigger causes a section of double-stranded DNA (a gene) to unwind into two single strands. With the help of a specific enzyme, messenger ribonucleic acid (mRNA) for tubulin is formed along one of the single strands of DNA. Through a series of reactions, the "message" sent from the DNA is translated. The "raw materials," amino acids, are lined up according to the message, and the needed protein is synthesized.

Now at The University of Texas Health Science Center at Dallas, Dr. Marcelle Morrison and Dr. Sue Griffin are able to probe the cells of the brain and see what proteins a single cell is producing. In a new combination of techniques, they have pooled their knowledge to become the first team to analyze individual brain cells not only for the presence of a specific protein but also for the presence of instructions – in the form of mRNA – to make that protein. If a neuron contains the specific mRNA for tubulin, the cell is making tubulin.

Morrison, associate professor of Neurology and assistant professor of Biochemistry, and Griffin, associate professor of Cell Biology, have previously found that immature brain cells contain more tubulin mRNA than mature cells do.

Until now they could find out only the total amount of tubulin present in tissue by grinding up a brain or a portion of a brain. But with these new techniques, the researchers can look at specific cells in brain tissue and see which individual cells are making which proteins. "We can now study the regulation of protein synthesis at the level of gene expression within a specific cell type and actually quantitate gene transcription on a per cell basis," says Griffin, a developmental neurobiologist.

"The cerebellum provides an excellent model for our studies because the timing of developmental events such as neuronal cell division, differentiation and migration have been well characterized. The layered architecture is geometric, and the neuronal circuitry is well documented."

The cerebellum is the part of the brain that controls fine muscle movement. Griffin compares the learning of a motor skill to "programming a computer."

"You can see a baby programming the cerebellum when you put a toy on its high chair tray. The first time it tries to pick it up, the hands oscillate and it knocks the toy off. Presently, the

cerebellum learns to judge how far to move the hand, how much to expand or contract the grasp."

In the adult, the cerebellum is calculating other fine measurements, for example in tennis playing: "Here comes the ball. How fast is it coming? Where should the racket be when it gets here? Do I need to move? What angle should I use?"

"When the skill is learned, the cerebellum just says, 'Okay, this is playing tennis,' and plugs in the almost infinitely modifiable program for playing tennis," says Griffin. "Outstanding athletes probably have an exceptional cerebellum or exceptional synapses (junctions between neurons)." If a person's cerebellum is damaged through disease, he or she must consciously think through every fine movement with no help from the cerebellum. The movements are never as good as when the cerebellum is working properly.

Different parts of the brain have different specific times of development. With the cerebellum, development begins before birth and continues at least through the first year of life in the human. In the rat, cerebellar development is compressed into a much shorter period and lasts for about three weeks after birth.

Development of the cerebellum begins with massive cell division followed by migration of the newly formed neurons to their permanent adult site. This developmental sequence was first documented in human cerebellar tissue early in this century by Ramon y Cajal.

What Morrison, a molecular biologist, and Griffin are now working toward is "the characterization of these developmental events at the molecular level."

With a single slice of brain tissue from a 10-day-old rat, the researchers first analyzed for specific proteins in the cells, using a complex procedure of tagging the proteins with specially treated fluorescent antibodies.

Then on the same slice of tissue, they successfully probed the brain cells for mRNAs by recombinant DNA tagged with radioactive molecules.

To obtain these DNA probes, they have constructed "libraries" of genes that code for all the cerebellar proteins of the human as well as of the rat. The individual gene copies (clones) can now be labelled with a radioactive molecule to become cellular probes in tissue from the cerebellum. Since the gene clones will pair only with their "matching" mRNAs, the presence of a "hybrid" of a gene clone for tubulin with the mRNA for tubulin, seen under the microscope, indicates that the cell was in the process of synthesizing tubulin. Cells that are dividing and using more tubulin will show more radioactive hybrids.

Now that Griffin and Morrison have perfected the technique, they can study the developmental activity of individual cells. They will focus on individual proteins involved in brain cell development, beginning with tubulin and actin, another protein involved in cell division and structure. Eventually, they want to know how the various events in brain development are triggered. It may be that each cell has its own internal switch, or the impetus may come from outside the cell. After a neuron has migrated to its adult site, input from other cells turns on the gene expression for the synthesis of enzymes responsible for the production of neurotransmitters.

Studies like these will some day enable researchers to attack previously unapproachable questions about abnormal brain development in the fetus and in the infant.

"Neurons are now thought to synthesize more than 100,000 different proteins," says Morrison. "If the synthesis of any one of these proteins is not properly regulated, the correct function of that neuron would be compromised.

"The isolation of gene probes to 'tag' mRNAs synthesizing important neuronal proteins can make it possible to study human and rat brain to learn how individual cells respond to stimuli by altering the synthesis of these mRNAs. This technique can be used to look at the brain cells of people with Alzheimer's disease to see why specific cells are dying and, therefore, why there is such a rapid and progressive loss of memory in these patients."

The gene probes can be used to study single processes in brain cells and thus identify a normal cellular function gone awry. At the same time, the gene responsible for the abnormal cell function can be identified. Once researchers identify it in the brain, the "bad" gene can be tested for clinically in any cell of the body – even in fetal cells through amniocentesis.

Some inherited degenerative neurological diseases such as Huntington's chorea and Joseph disease show up in middle age after people have had their children. At present, there is no way to predict who will develop these diseases. If family members of patients could be tested for the gene, those with the disease could choose not to have children. And, eventually, these diseases would die out.

At present, there is no way to predict who will develop these diseases. If family members of patients could be tested for the gene, those with the disease could choose not to have children. And, eventually, these diseases would die out.

Another frightening disorder, Alzheimer's disease, is not clearly a genetic disease, but there is a higher incidence among family members of patients. If an abnormal gene is found to start the death of brain cells in this disease, the gene responsible could be tested for in the fetus.

Griffin and Morrison are now making plans with clinical researchers to use their technique to study fragile X chromosome (a cause of mental retardation) and Alzheimer's disease.

"All these clinical developments are a long way off," says Griffin. "But they are now possibilities."

"Our libraries are about the only way to study anything as complex as the nervous system," says Morrison. "Obtaining a gene for a specific protein and using it as a cellular probe for one mRNA out of 100,000 provides the magnet to pull the needle out of the haystack." ♦

CAPSULES

New treatment for that old knee injury

The knee is the focal point of many new medical discoveries in the field of sports medicine, a specialty in orthopedics spawned by the continued popularity of organized sports combined with the nation's obsession with fitness. Orthopedics is currently one of the most popular specialties in medicine today, according to Dr. Richard Jones, an orthopedic surgeon at the health science center responsible for teaching and recruiting residents. Says Jones: "There were eight applicants for every available (residency) position last year. Everyone is interested in athletics and the field is really expanding."

Thus, with such a concentration in the field, it is not surprising that tremendous gains have been made in sports medicine, now a sub-academy of The American Academy of Orthopedic Surgeons.

Sports medicine encompasses state-of-the-art technology to condition, diagnose, treat and rehabilitate athletes. Some of the advancements are:

♦ **Arthroscopy** – a diagnostic and treatment technique in which the surgeon enters a joint with a small scope (about the size of a pencil) to view the structures of the joint, particularly the ligaments and cartilage (a dense, connective tissue covering the bone ends and providing the smooth, gliding surface). With the arthroscope, operations can be performed without surgically opening the knee. There is a 95 percent diagnostic accuracy rate with arthroscopy compared to a 70 percent accuracy rate using conventional methods (history, exam and X-ray). Designed in Japan in 1970, the procedure was introduced in this country in 1972 and has since undergone several modifications.

Arthroscopy is most effective in the diagnosis and management of lesions of the meniscal cartilage ("shock absorbers" within the knee that serve to evenly distribute the forces and loads applied to the articular cartilage, or gliding surface, of the knee). The meniscus is frequently damaged in athletics and may actually impinge between the joint surfaces and cause erosion or prevent full motion, says Jones.

Arthroscopy can also be used as an adjunct in evaluating severe ligamentous injuries that occur when a joint is forced into an unnatural position, ripping the ligament. Traditionally a surgeon could sew the ripped ligament back together and hope that it would heal in the shortest possible position. If not properly repaired, however, or with repeated surgeries, a knee has "slop" in it instead of moving smoothly and synchronously throughout a full range of motion. The knee then shakes and shimmies on the articular cartilage, wearing it down, resulting in degenerative changes. Arthroscopy can assuage the symptoms of the degenerative changes by smoothing out the shaggy articular cartilage and trimming up any other mechanical blocks to joint function.

♦ **Artificial ligaments** – significant progress has been made in reconstruction of injured ligaments. In the past, athletes resigned themselves to loose, wobbly knees. But today, athletes in disrepair may again walk on legs that support them. Two new forms of artificial ligaments have gone into experimental evaluations in selected patients, according to Jones.

One product is artificially made with carbon and the other is made from cow ligament (from the back of a cow's head).

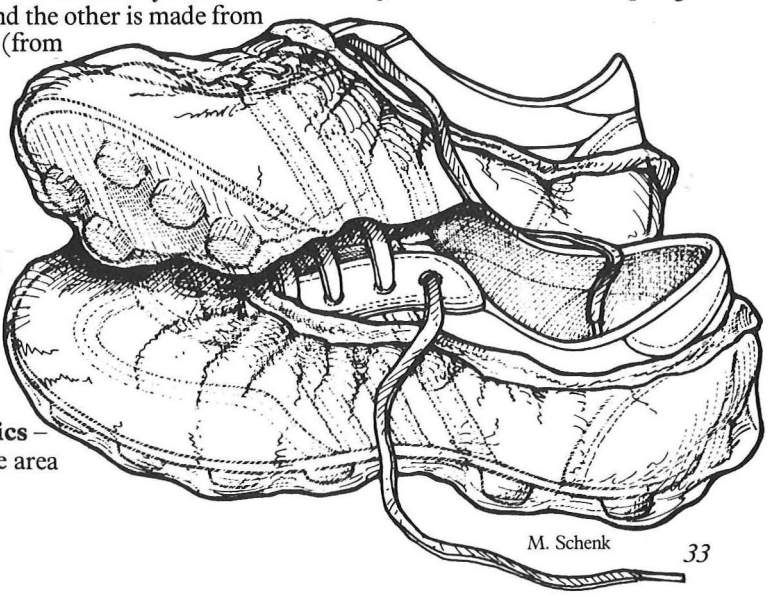
Prime candidates for artificial ligaments are athletes suffering chronic ligamentous injuries or repeated trauma to the knee joint.

♦ **Orthotics** – research in the area of immobilization of limbs in the post-operative phase indicates motion is good for the knee joint. Whereas yesterday's recovering athletes wore casts to immobilize the knee, new orthoses (external devices offering support of weakened or injured limbs that allow movement are preferred.

Improvements in braces worn by athletes after return to activity have also increased functional performance.

♦ **Rehabilitation** – electrical muscle stimulation is applied through pads over muscles to strengthen motor muscle units and the knee after surgery. Shooting an electrical charge into weakened muscles stimulates the nerves, causing a full muscle contraction. Perfected by the Russians and East Germans for the 1972 Olympics, this method has been available in the U.S. for several years. If a nerve is cut, the muscle surrounding it can't function, so electrical stimulation can also keep the muscle tone until the nerve grows back, says Jones.

Used to rehabilitate or condition athletes, the procedure is most effective if the patient receives stimulation while actively exercising against resistance. A program consisting of 10 contractions a day, five days a week will enable a patient to achieve full muscle strength, according to Neal Hughes, a physical therapist at the health science center and former member of the Olympic Training Center in Colorado Springs.



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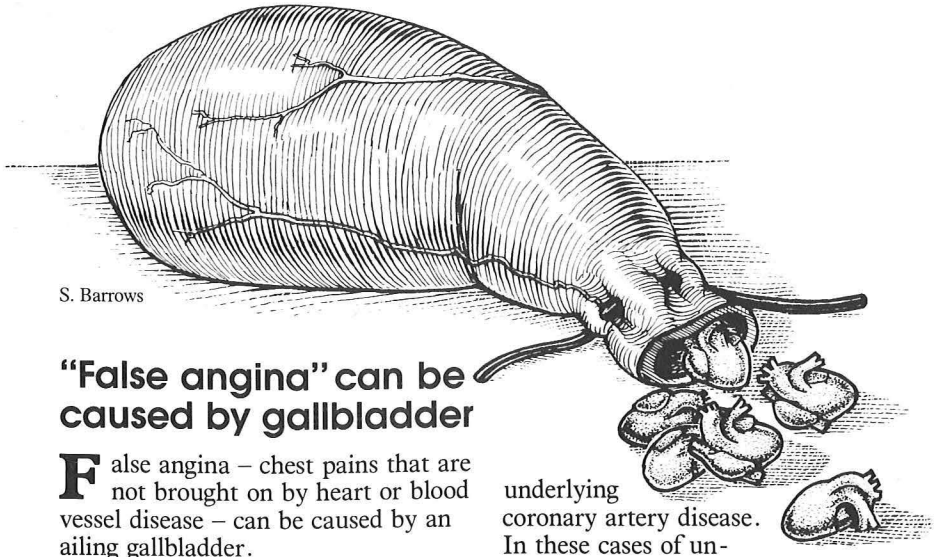


S. Barrows

"False angina" can be caused by gallbladder

False angina – chest pains that are not brought on by heart or blood vessel disease – can be caused by an ailing gallbladder.

Cardiovascular physiologist Dr. George Ordway at the health science center is examining the link between a diseased gallbladder and chest pain.

Located under the liver, the gallbladder is a repository for bile produced by the liver and used for breaking down fats. When the gallbladder becomes diseased by crystal formation (gallstones) or infection, pain is usually felt as abdominal pain. Sometimes, however, gallbladder pain follows nerve pathways up the spinal cord to become "referred pain" felt in the chest area. This could allow a person to think they are suffering from heart disease when they are not, says Ordway.

The possibility also exists that cardiovascular reflexes originating in the gallbladder could produce an added stress to the heart of someone with underlying coronary artery disease. In these cases of underlying heart disease, problems of the gallbladder could stimulate the heart into producing true angina.

"The only way of determining the origin of anginal pain is by contacting a physician," says Ordway, whose work is funded by the American Heart Association, Texas Affiliate.

The researcher's work involves the use of bradykinin, a substance that is found in the body and is associated with pain and inflammation. Present also in bile, bradykinin can stimulate sensory nerves arising from the gallbladder to increase blood pressure, heart rate and the force with which the heart contracts. The result is an increase in the work done by the heart. "A normal heart should be able to meet the demands of extra work placed on it if this happens," says Ordway.

Copper stimulates release of LHRH

The trace metal copper found in the body stimulates the release of a hormone essential to ovulation. In the first reported study of the effects of copper salts on nerve cell granules isolated from the brain of rats, Dr. Ayalla Barnea and Dr. G. Howard Burrows found 17 times as much luteinizing hormone releasing hormone (LHRH) released from granules incubated with copper as was released from control granules.

Barnea, associate professor of Obstetrics and Gynecology and Physiology in the Cecil H. and Ida Green Center for Reproductive Biology Sciences at the health science center, presented their findings at the annual meeting of The Endocrine Society.

"Our study strongly suggests that copper acts directly on hypothalamic granules to release LHRH," says Barnea.

LHRH, a peptide composed of 10 amino acids, is produced in nerve cells located in the hypothalamus (an area of the brain). The hormone is secreted from the hypothalamus directly into the blood supply of the pituitary gland, causing the pituitary to secrete the hormones luteinizing hormone (LH) and follicle stimulating hormone (FSH). These two pituitary hormones are essential for the normal function of the ovaries in the female and the testes in the male.

In a cell, peptide hormones are stored within granules, protected by a membrane, until something triggers a series of events to get the hormone to the outside of the cell.

Neurosurgery benefits some with epilepsy

Twenty pills a day couldn't suppress 18-year-old Keith's epileptic seizures. The medication blurred his thinking, dulling his personality. Averaging eight seizures a day, he suffered the crippling embarrassment of losing control of his body in public.

Keith's seizures ended recently when a pecan-sized, grey lump was surgically removed from the left side of his brain. Laboratory analysis revealed the growth was not cancerous. It was a blood vessel abnormality probably present from birth.

Neurosurgeon Dr. John Mullen, epilepsy specialist at the health science center who performed the surgery, says that brain surgery can benefit about half the epilepsy patients whose seizures don't respond to anti-convulsant drugs. Of the two to four million people in the U.S. living with chronic recurrent seizures, one tenth can be considered for surgery, he says.

Mullen is one of a small group of neurosurgeons in this country with extensive training in surgical procedures to locate and remove epileptogenic (seizure-producing) tissue. Multiple electroencephalograms (EEGs) are used both prior to and during surgery to identify irregular brain waves and to locate the focus of the seizures. In Keith's case, Mullen says the growth itself had not produced the seizures. It was damaged tissue around the growth that had erratically discharged electrical activity throughout the brain.

"Highly epileptogenic tissue is not functioning brain and will only produce a worsening of symptoms if left alone," says Mullen.

Surgery begins after lengthy testing has determined the location of the speech and other vital centers. These sensitive areas are carefully avoided during surgery. An EEG is used to guide the surgery and to define the lesioned areas and indicate how much tissue should be removed.

After the epileptogenic tissue has been removed, the skull flap is replaced and the patient is closely monitored for the next few weeks to check for recurring seizures.

Mullen is working toward a comprehensive epilepsy care program for patients with seizure disorders, including medical, surgical and psychological management.

Fluid in the ears may cause learning problems

The first few years of life are crucial to a child's learning. But many children may be missing out on what is going on around them at this time, says Dr. William Meyerhoff, chairman of Otorhinolaryngology at the health science center.

Fluid in the ears of these children causes a loss of hearing that affects their personality, behavior and educational growth in ways that are just beginning to be recognized. And many of these children lack the familiar symptoms of ear infection – fever, crying, holding the ears.

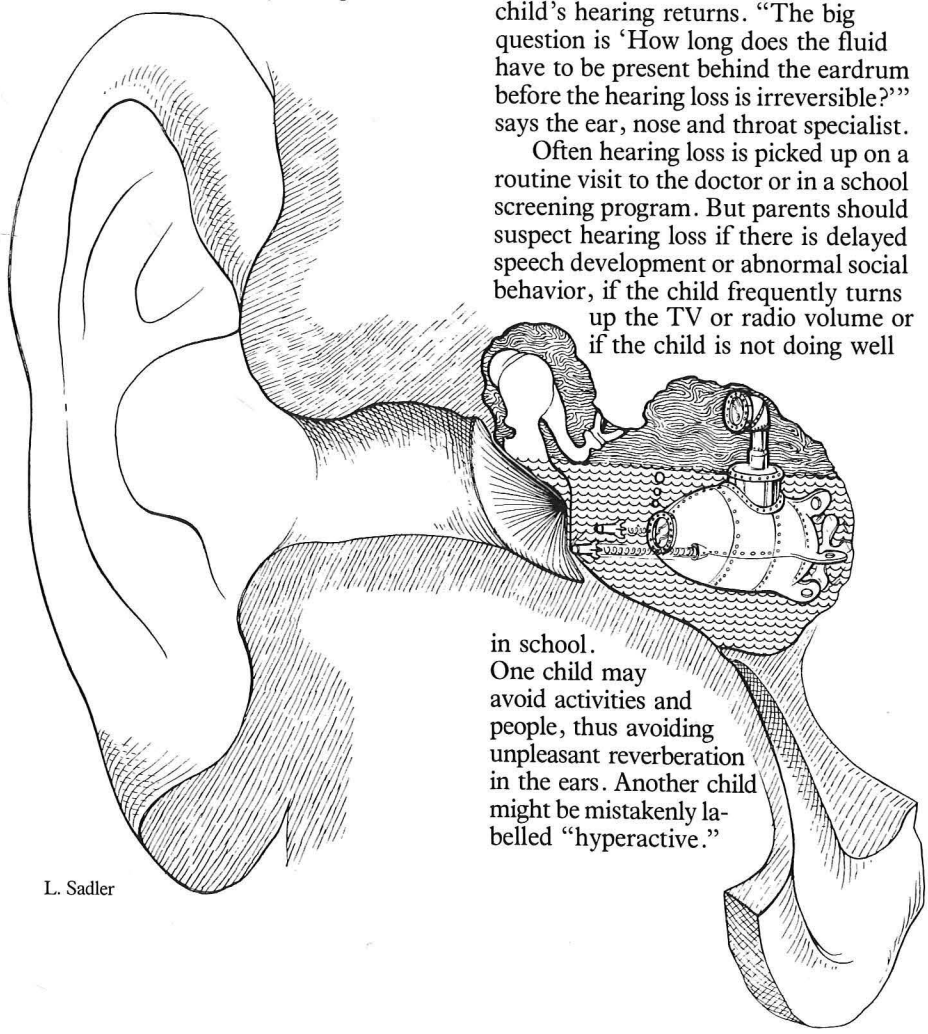
Meyerhoff is a strong believer in the use of tympanostomy tubes (tubes through the ear drum) as a temporary measure to relieve children with chronic ear infection. This almost always reverses hearing loss, he says.

Children who have been treated surgically with the tubes often show beneficial personality changes as a result. "One little boy used to sit in the corner and play by himself. When his mother brought him back for a checkup, she reported that he was now 'into everything,' " says Meyerhoff. "Of course, he didn't want to interact with his environment before. He didn't feel a part of everything around him."

Fluid in the ear feels a lot like having the ears stop up on an airplane or in the mountains – only about 10 times worse. While the fluid is present, there is hearing loss, but there is also an echoing of sound so that all the sounds one hears are mixed up. Adults with fluid behind the eardrum know that something is wrong and seek immediate action. But a child who has had the condition for a long time may not know how it feels to have normal hearing. And if there is no pain or fever, the condition may be missed.

Seventy-five percent of children at age six have experienced hearing loss because of fluid in the ear. Some of the hearing loss is transient. It's a "mechanical thing." When the fluid is present, the child has hearing loss. Usually when the fluid is removed, the child's hearing returns. "The big question is 'How long does the fluid have to be present behind the eardrum before the hearing loss is irreversible?'" says the ear, nose and throat specialist.

Often hearing loss is picked up on a routine visit to the doctor or in a school screening program. But parents should suspect hearing loss if there is delayed speech development or abnormal social behavior, if the child frequently turns up the TV or radio volume or if the child is not doing well in school. One child may avoid activities and people, thus avoiding unpleasant reverberation in the ears. Another child might be mistakenly labelled "hyperactive."



L. Sadler

Dermatologists explore defenses against disease

Research efforts within the newly established Department of Dermatology at the health science center concentrate on several unique ways the skin deals with disease. A National Institutes of Health-sponsored Center of Immunodermatology, headed by Dr. James Gilliam, who is also department chairman, funds the group's investigational projects probing cancer, lupus erythematosus, psoriasis, allergies and other skin-related diseases.

Lupus erythematosus, a sometimes deadly disease afflicting 500,000 Americans, 90 percent of them women, is being examined by lupus authorities Gilliam and Dr. Richard Sontheimer. Known as a multi-system disease, lupus sometimes affects the skin with a characteristic butterfly-shaped rash on the nose and cheeks. It can affect practically every organ by causing inflammation in connective tissue, the material giving strength to all tissues. Inflammation can occur in sites throughout the body.

Using the skin as an indicator, Gilliam and Sontheimer have developed classifications for the clinical spectrum of lupus. Subsets range from the mildest forms of lupus with skin involvement only to the most lethal forms of whole body disease. Skin manifestations, they found, can indicate the extent of system involvement. And greater concentrations of antibodies in apparently normal skin are found in the more severe forms of lupus.

Another member of the research team, Dr. Paul Bergstresser, has observed that the tanning rays of the sun, called "ultraviolet B" or "UVB," can cause the skin's immune system to fail to function. In experiments involving giving low doses of UVB to mice, Bergstresser and his associates found that, once irradiated, the mice did not develop a normal immune response when painted with chemicals resembling the toxin in poison ivy. Swelling, the normal immune response in mice, failed to occur.

The same thing may be true in humans, says Bergstresser. It is possible that a similar disruption of immune response by natural sunlight could contribute to the development of skin cancer.

Five lives touched by one death

Within days of David Glisson's death, five lives had been touched by his generosity and compassion for other people. The same Saturday that his family and friends were assembled for a memorial service at a Duncanville Baptist Church in order to celebrate the life of this young man, surgeons in a Dallas hospital were performing a bone transplant made possible by David's gift. Because of the 19-year-old's decision to be a transplant donor and his family's respect for their son's intent, three men have been given a chance to walk normally again, a woman who lives in a different part of the country may regain her sight, and the victim of an explosion with massive burns was helped in his fight for life by a skin transplant.

It was David's father who remembered his son's wish to donate his organs. David had to have a kidney removed when he was 16. After that time, Glisson said, his son was always conscious of the fact that if anything went wrong with his remaining kidney, he would be dependent on the generosity of a donor and the availability of an organ.

According to Dr. Charles Baxter, this is the first time that six transplants from one donor have been attempted within such a short period of time. (One cornea could not be used because of medical problems.) Baxter is head of the Parkland Burn Center and medical director of the related "bankable" organ transplant program at the health science center. ("Bankable" organs are those that may be stored for transplant at a later time.) Currently the program handles donations of corneas, skin for burn and other victims of large traumatic wounds and bones used in hip, knee, back and jawbone operations. It is the first and, currently, the only transplant program dealing with multiple-organ donation as a coordinated effort although it is serving as a prototype for other centers interested in setting up similar units.

Baxter and his associates are in charge of the largest skin-banking effort in the country and have long been involved in eye-banking for cornea transplants and research. Bone-banking is a more recent involvement, beginning with the addition to the faculty four years ago of Dr. Marvin Meyers, an orthopedic surgeon who is one of a handful in the country who perform these still-experimental surgeries. Meyers, a pioneer in bone transplants, has done 38 knee and 21 hip transplants in the past eight years. The first surgeon to perform a hip transplant, Meyers now heads one of only six teams performing these surgeries in the U.S. and Canada.

The bankable organ transplant program has donor cards available, and state law permits citizens to express their wishes to donate organs by signing an indication of intent on the back of their driver's license. However, the most important thing is for potential organ donors to make sure their families understand this intention, said Ellen Heck, coordinator of the transplant program. Her office can be reached for information by writing the health science center or dialing 214/688-2609.

Salt to taste

The average American adult consumes 10 to 12 grams (two and one-half to three level teaspoons) of table salt (sodium chloride) each day, says Dr. Norman Kaplan, a nationally recognized hypertension expert and professor of Internal Medicine at UTHSCD. As he emphasizes in his new book *Prevent Your Heart Attack* (Scribners and Sons, New York), salt was originally used as a preservative before refrigeration. As carry-overs, we still have salt pork, beef jerky, pickles and sauerkraut. Salt is not needed as a preservative any longer – packaging and refrigeration are much more important in preserving foods, says Kaplan. But now salt is added to almost everything for taste.

"We assume a taste for salt is a learned thing," says Kaplan. "There is no physiological need for the large amounts of salt we are now eating."

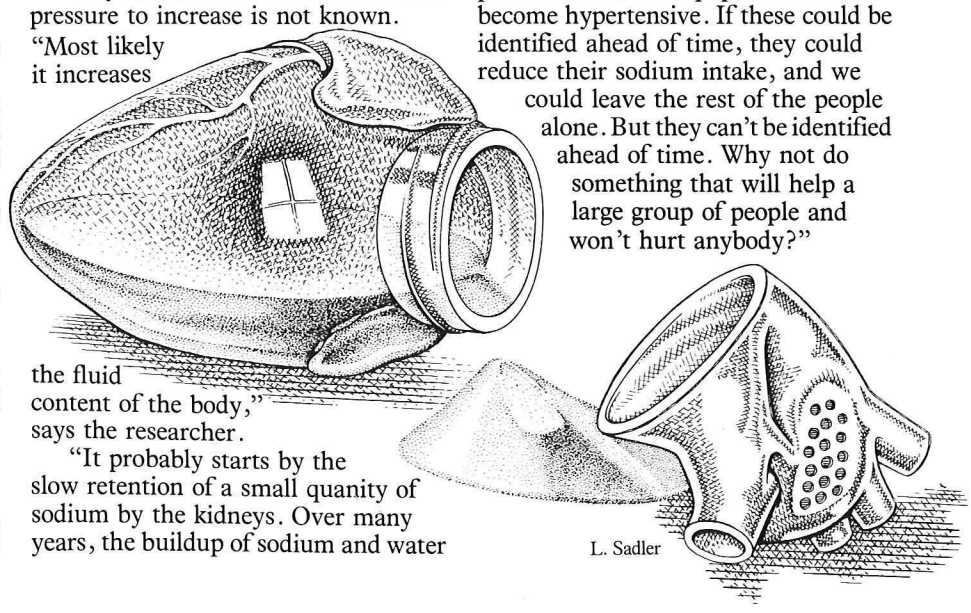
The problem with having a taste for salt is that hypertension may be caused by a slow build-up of sodium in the body. It is not certain that this is the case, but more and more evidence points in this direction. For one thing, cutting down on the sodium intake will lower the abnormally high blood pressure – even without medication. In patients taking medication for hypertension, sodium restriction will reduce the blood pressure even further.

"Some primitive tribes of people have a low sodium and a high potassium diet and also have a low incidence of hypertension. A high potassium diet may actually protect against high blood pressure," says Kaplan.

Why sodium would cause the blood pressure to increase is not known. "Most likely it increases the fluid content of the body," says the researcher.

"It probably starts by the slow retention of a small quanity of sodium by the kidneys. Over many years, the buildup of sodium and water over-fills the circulatory system and causes the blood pressure to rise. In an attempt to protect themselves from the heightened pressure, the arteries develop thicker walls. This limits their capacity and further raises the pressure."

Some researchers believe there is no need for normal people to reduce their sodium intake. Kaplan, however, comes down strongly on the side of general sodium restriction. "Twenty percent of the U.S. population will become hypertensive. If these could be identified ahead of time, they could reduce their sodium intake, and we could leave the rest of the people alone. But they can't be identified ahead of time. Why not do something that will help a large group of people and won't hurt anybody?"



L. Sadler

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