GRADING AREA HIGH SCHOOLS • LIFE AS A REDSKIN

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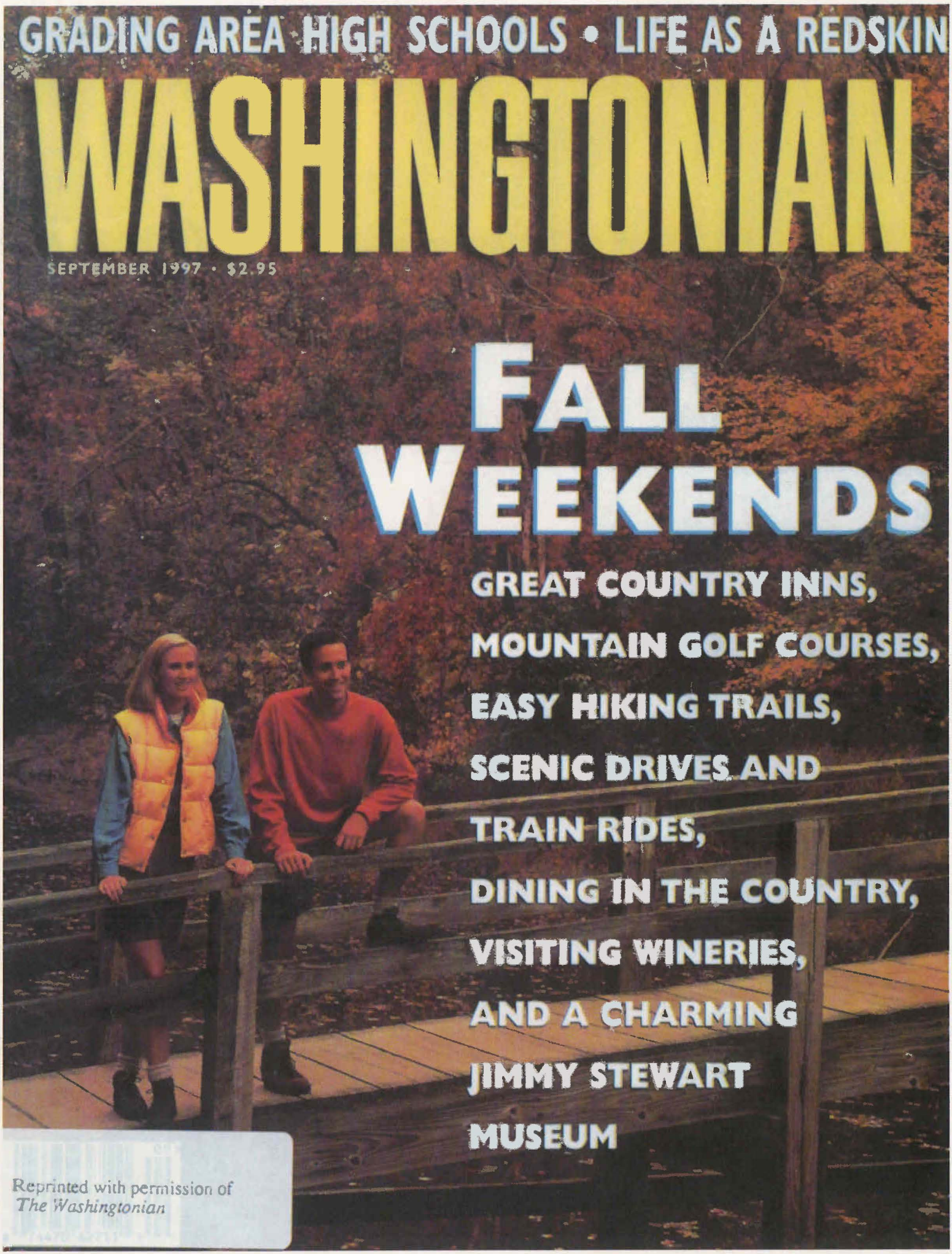
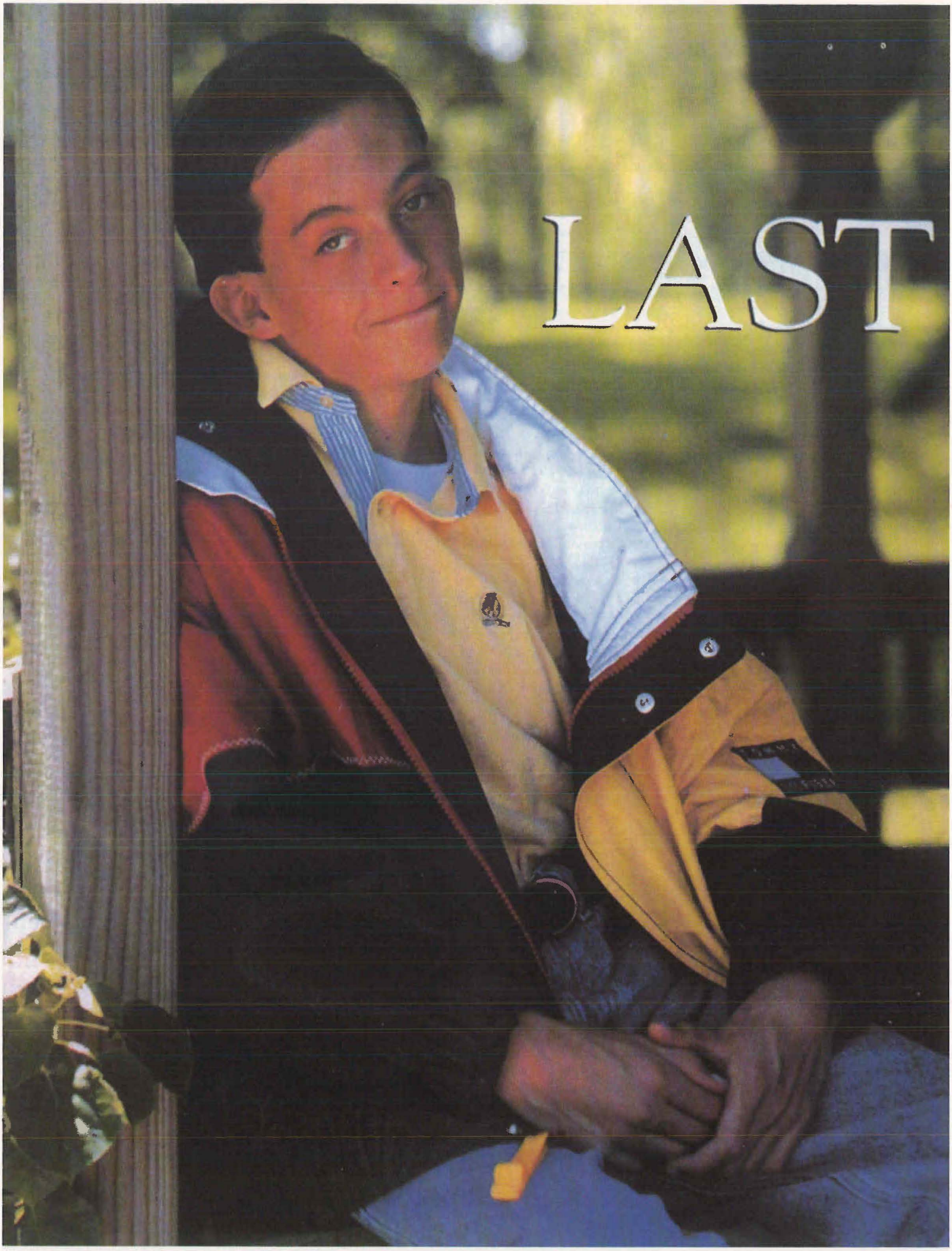


FALL WEEKENDS

GREAT COUNTRY INNS,
MOUNTAIN GOLF COURSES,
EASY HIKING TRAILS,
SCENIC DRIVES AND
TRAIN RIDES,
DINING IN THE COUNTRY,
VISITING WINERIES,
AND A CHARMING
JIMMY STEWART
MUSEUM


LAST

THEY HAVE RARE DISEASES, BIZARRE CONDITIONS.

SOME HAVE ONLY MONTHS TO LIVE.

THEY COME BY THE THOUSANDS TO NIH

IN BETHESDA, YEARNING TO BE CURED.

BEST HOPE

BY LARRY VAN DYNE PHOTOGRAPHS BY BARBARA RIES

JASON SHAFT AND HIS MOTHER, Linda, have taken an evening flight from Louisville to BWI and grabbed a taxi to the National Institutes of Health, the federal government's medical-research complex in Bethesda. The driver drops them off at about 9:30 in front of the Children's Inn at NIH, which provides free lodging for families with children undergoing treatment there. They quickly unpack their suitcases, pick up sheets from the linen closet, and make their beds.

They are accustomed to this routine—it's their tenth visit to NIH in the past eight months—but Linda Shaft is worried this trip about a pivotal medical exam Jason will undergo the next morning. She cannot get it out of her mind as she watches her only child—a bright 15-year-old who has been ill nearly all his life—fall asleep across the room.

The Shafts, who live in the little town of Shepherdsville, Kentucky, have known since Jason was two months old that he suffers from a genetic disease called neurofibromatosis-type 1. The illness was recognized at a Louisville hospital where they took him because he was underweight and suffering from a severe cold.

Neither Linda nor her husband, Kevin, had ever heard of NF-1, and they were taken aback when the geneticist asked which of them also suffered from the disease and had passed it on to Jason: "Which one of you is it?"

To the geneticist the answer was obvious from a glance at Kevin's back, which bore a big brownish spot that Kevin had always thought was a birthmark but was actually one the disease's telltale signs. It was a complete surprise to Kevin, because he suffered from none of the disease's worst symptoms.

Jason Shaft, a 15-year-old from Kentucky, has nonmalignant—but life-threatening—tumors growing throughout his body. It's always a tense time when he comes to NIH in Bethesda to see if the drug he's been given is having an effect.

JASON HAS NOT BEEN SO LUCKY. Tumors grow along his nerves, in bead-like chains just under the skin and deeper along his spinal column, in his neck, and near his internal organs. These growths—ranging from the size of a pea to the size of a peach—are not malignant, but they could become so. He also has scoliosis (curvature of the spine), which has left one shoulder higher than the other, and he suffers from hearing loss—65 percent in one ear, 25 percent in the other. He has always been short for his age, due to a pituitary-gland dysfunction, though treatment with growth hormones has helped him add 17 inches in the past four years. He's now five-foot-three.

Since no drug has proved effective in destroying NF-1 tumors, the only real option is surgery, which Jason has undergone on five occasions. The first, when he was four, was done in Louisville after an orthopedist noticed a difference in the size of Jason's feet—a clue that tumors were interfering with nerves along his spinal cord.

When he was 12, another mass of tumors in his lumbar region was removed at another hospital. During that procedure, he suffered an injury that left him blind in his right eye.

Since then he's had tumors removed at hospitals in Louisville and Memphis and at Children's National Medical Center in Washington, where he also was enrolled in a clinical trial of a drug that proved ineffective in slowing tumor growth.

Though Kevin Shaft continues working as a trucker, Linda quit her job as a program director at a YMCA to devote much of her time to Jason and his illness. One of the duties she's taken on is keeping abreast of research developments and staying in touch with experts like Dr. Roger Packer, one of Jason's doctors at Children's. After returning to Kentucky, she called Packer every few weeks with the same message: "If there's ever any study Jason might qualify for, please don't forget him."

IN JULY OF LAST YEAR PACKER called to say that a new study at the National Cancer Institute, where he served as a consultant, might offer some hope. The study was designed to test the safety of a drug called phenylacetate on children with malignant brain tumors, one of the most difficult cancers to cure.

NIH was willing to treat Jason in the study because his tumors, while not malignant, were life-threatening and had so surrounded his blood vessels, nerves, and organs that they were no longer operable.

Jason began receiving the drug in August of last year. For 28 days at a stretch he wears a fanny pack that contains an intravenous bag and a pump that delivers the drug through a catheter in his chest, and he comes to the National Cancer Institute periodically to assess whether the drug has had any effect on the growth of his tumors. He has hundreds of them throughout his body, but Dr. Peter Adamson, the study's principal investigator, has settled on about ten larger ones in his neck and along his spine for monitoring. They're checked by a magnetic-resonance-imaging machine, which offers a view of the body's interior that was unthinkable just a generation ago.

Tomorrow morning, after Jason awakes at the Children's Inn, he'll go up the hill to the hospital and lie inside the MRI unit for more than four hours while his mother waits outside for the news. →

Let the Sick Be Healed

NIH IS ONE OF THE REGION'S PREeminent institutions, and its presence in Bethesda is both a case of felicitous symbolism and an accident of history. The symbolism arises from the Bible, in which Bethesda is the Hebrew name of a great pool of water in Jerusalem blessed by an angel with the power to heal the impotent, the blind, the halt, and the withered. The accident of history dates from the mid-1930s and was set in motion by a wealthy Washington couple—Luke Wilson, whose money came from a sporting-goods store in Chicago, and his wife, Helen, the daughter of a founder of Washington's own Woodward & Lothrop department store.

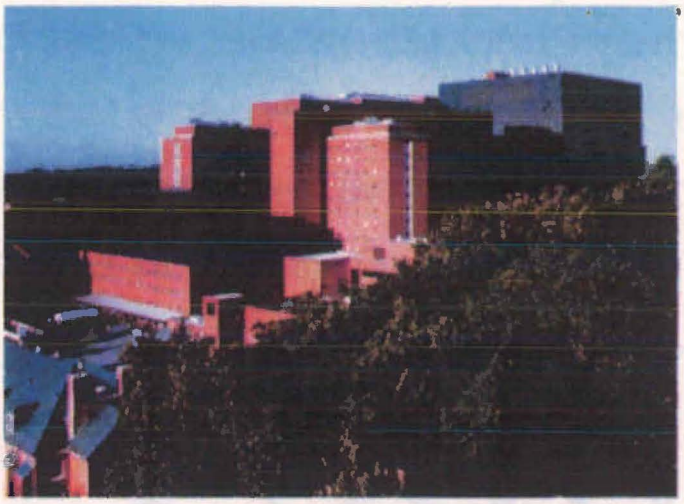
In 1935 the Wilsons offered to donate half of their 94-acre "Treetops" estate in Bethesda to the federal government, a gift that fell eventually into the hands of the National Institutes of Health, then a small federal agency operating out of a few buildings on a hilltop just east of where the Kennedy Center now stands. Though NIH first intended only to build a facility on the Wilson estate to house animals used in experiments, it moved its entire operation there by the late 1930s and has added land through gifts and purchases.

The NIH campus now encompasses just over 300 acres, between Rockville Pike and Old Georgetown Road, and is covered not only with groves of mature trees but with more than 50 buildings. NIH has 18 institutes under its purview, all but a handful with research operations here and each devoted to a certain disease or medical discipline.

The oldest and by far the largest, with almost a fifth of the NIH budget, is the National Cancer Institute, which was created in 1937. Six others trace their origins to the years immediately after World War II—Heart, Lung, and Blood (1948); Allergy and Infectious Diseases (1948); Dental Research (1948); Mental Health (1949); Diabetes and Digestive and Kidney Diseases (1950); and Neurological Disorders and Stroke (1950).

Newer institutes have arisen out of congressional mandates, the political clout of disease lobbies, from heightened consciousness of certain health problems, and from the advancement of scientific technology. Among the institutes created in the 1960s were Child Health and Human Development (1962), General Medical Sciences (1962), the National Eye Institute (1968), and Environmental Health Sciences (1969), which is based in North Carolina's Research Triangle.

Since then have come Aging (1974) and Drug Abuse (1974), both of which do the bulk of their work in Baltimore; Alcohol Abuse and Alcoholism (1974); Arthritis and Musculoskeletal and Skin Diseases (1985); Deafness and Other Communication Disorders (1988); and Nursing Research (1993). The National Human Genome Research Institute, whose origins date to 1989, is involved in the exciting field of human genetic research, and new units have been added in recent years on AIDS research, women's health, and alternative medicine.



Patients from across the country get cutting-edge medical treatment in about 900 studies, involving dozens of diseases, at NIH's Clinical Center in Bethesda.

THE FACT THAT NIH IS A CREATURE of the federal government is obvious from the names on the sides of its buildings—names that reflect Washington's culture of bureaucracy and politics. Each building is assigned a number as impersonal as the prose of the *Federal Register*—Building 1 houses the central administration, Building 6 has laboratories for the National Cancer Institute, and Building 28 is a hospital for animals used in research. But several of these buildings also bear the names of congressmen and senators who have served as promoters of the NIH budget—from Claude Pepper, the New Dealer from Florida who is often considered the legislative father of NIH, to Lister Hill of Alabama, John Fogarty of Rhode Island, Silvio Conte of Massachusetts, William Natcher of Kentucky, Lowell Weicker of Connecticut, and Warren Magnuson of Washington.

In the organization chart of the federal government, NIH falls within the Public Health Service, which in turn is part of the Department of Health and Human Services. Its annual appropriation provides about 31 percent of all the money for medical research in the United States, with another 52 percent coming from drug companies and the rest from other federal agencies, states, foundations, and other sources.

Federal spending on medical research has risen dramatically since World War II, and this year the NIH budget is about $12.7 billion. That's only slightly less than spending on NASA ($13.7 billion) or the Energy Department ($14.2 billion). With about 16,000 employees in Bethesda, NIH is also one of the engines of the Montgomery County economy—a magnet, like the Food and Drug Administration in nearby Rockville, in the county's effort to attract companies in the emerging field of biotechnology.

NIH spends about 6 percent of its budget on its central administration in Bethesda and another 11 percent on research there, but the bulk of its money, about 83 percent, is sent out via grants to university medical centers around the country. The competition for these peer-reviewed grants is tough and getting tougher—only 28 percent of the 24,000 grant proposals received last fiscal year were funded. Johns Hopkins University in Baltimore got the most money ($279 million), followed by the University of California at San Francisco ($213 million), the University of Washington ($212 million), and the University of Pennsylvania ($187 million). Locally, Georgetown got $43 million and George Washington $24 million.

This national scope also is apparent in the distribution of Nobel Prize winners whose research was supported by NIH grants. Four did their work in Bethesda, but 88 did theirs elsewhere, including Harold Varmus, a cancer researcher from California who assumed the post of NIH director in 1993.

SOME OF THE WORK GOING ON IN Bethesda is "basic research"—studies limited to the laboratory or to animals and aimed at understanding the human body and its diseases at the most fundamental level. But there's also a lot of "clinical research," which involves patients like Jason Shaft who are willing—and often eager—to volunteer for studies of diseases and experimental treatments.

For them the heart of NIH is Building 10, the 14-story hospital that is also known as the Clinical Center and sits in the middle of the campus. All patients, regardless

BUILDING PHOTOGRAPH COURTESY OF NIH

Virginia Via has spent 90 weeks at NIH so doctors could study her Alzheimer's disease. To pass the time, she has crocheted 30 afghans.

of their disease or the institute that's studying them, are routed through this building for tests or treatment. Opened in 1953—the first patient was a 67-year-old farmer from Gaithersburg with prostate cancer—the Clinical Center is named in honor of the late Warren Magnuson, the legislator from Washington who was a longtime champion of NIH. A multimillion-dollar renovation and expansion—just now beginning—also will honor another NIH supporter, recently retired Senator Mark Hatfield of Oregon.

The Clinical Center is not intended to handle the patient load of a community hospital; its 7,000 inpatients and 68,000 outpatients last year were far fewer than the 44,000 inpatients and 139,000 outpatients at Inova Fairfax Hospital, one of the Washington area's busiest. The Clinical Center is nevertheless a formidable institution—a brick-and-glass monolith that includes 325 beds for patients, hundreds of rooms, and nine miles of corridors. The staff includes 1,200 physicians, dentists, and PhD scientists as well as 660 nurses and 540 others, ranging from dietitians and medical technologists to therapists and pharmacists. The clinical pathology department on the second floor is the size of a football field, and the pharmacy dispenses about 40,000 capsules and tablets each day.

To accommodate patients who come from all over the country, NIH operates a shuttle bus from National and BWI airports, and it has a travel agency in the lobby to book flights. The Children's Inn has rooms for 36 out-of-town families. On the top floor of the Clinical Center there's also a gymnasium, an exercise room, a playroom for kids, an auditorium, and a chapel, which features a wall hanging based on the story of Bethesda in the Bible.

BUT IT'S WHAT THE CLINICAL CENter does not have—no emergency room, no obstetrics ward—that provides a clue to the unique nature of the place. It is a research hospital in the deepest sense, so poised on the cutting edge of medical science that ordinary cases, like that of a construction worker who breaks an arm while working on campus, are referred to nearby Suburban Hospital. This special mission is reflected in the Clinical Center's "bench-to-bed" design, with laboratories where scientists work at waist-high benches placed across the hall from patient rooms. And while other hospitals do clinical research, no other hospital in the world has so many research beds at its disposal.

That distinction—along with the Clinical Center's federal status, its record of accomplishment, and its ability to draw patients from across the country—gives it a claim to the title of America's Hospital.

Nearly 21,000 of its patients—just over half—come from the District, Virginia, and Maryland. Of those, Maryland alone accounts for 12,800. But every other region is well represented—2,200 from California and elsewhere out West, 3,800 from the Middle West and Great Plains, 4,000 from the South, and 5,800 from New England, New York, and Pennsylvania.

Patients come from all walks of life, rich and poor. This being Washington, the patient mix includes politicians and other VIPs, from the late Billy Carter (pancreatic cancer) and the late Oklahoma Congressman Mike Synar (brain cancer) to ABC television journalist Sam Donaldson (melanoma).

Like Jason Shaft, they often suffer from illnesses that have ruined their lives or threaten their existence. Often they are referred to NIH as a last chance. Filled with the same desperation that brought the sick and dying to the healing pool of ancient Bethesda, they come with the hope that modern science can make them whole.

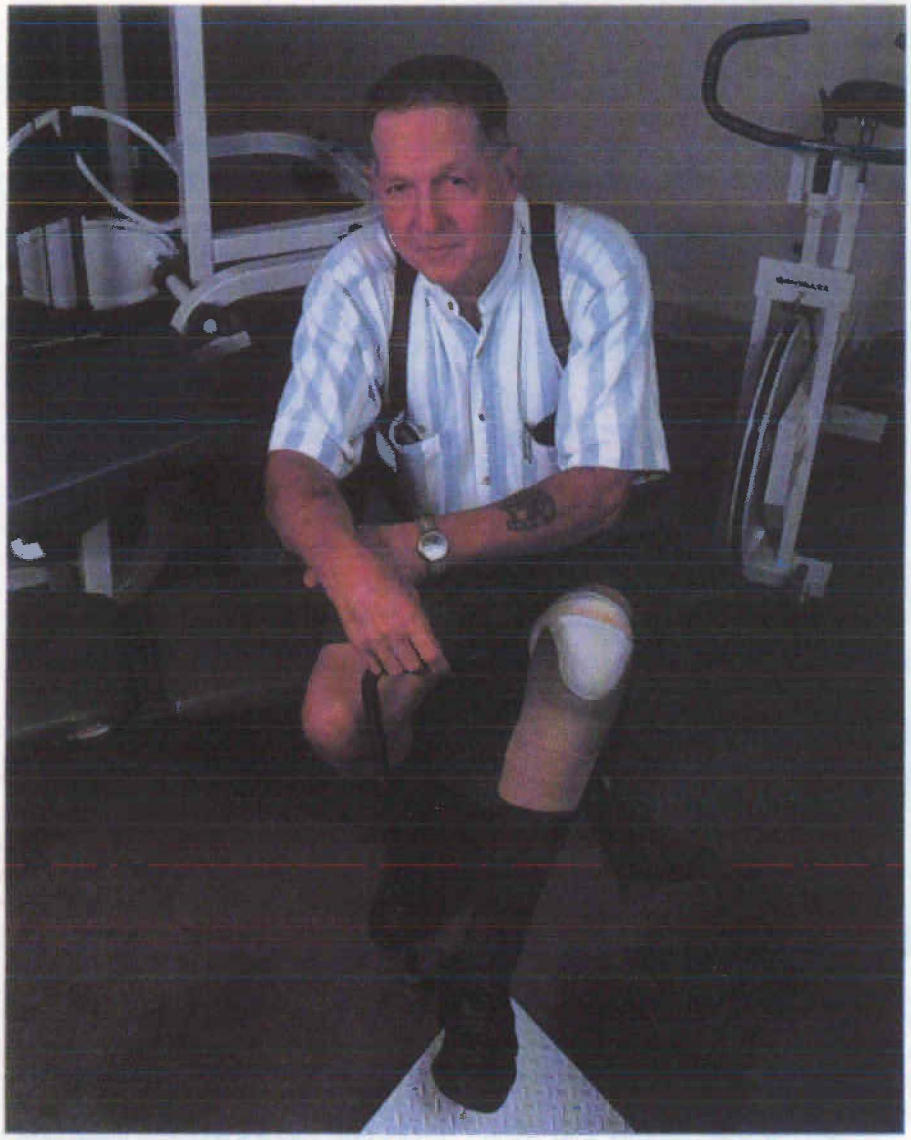
Lost Memory

VIRGINIA VIA, AGE 83, IS A CHARACter from an era in Washington life that has faded away. Her late husband worked as a conductor on some of the last of the city's trolley cars. And she was once manager of the beauty salon at Woodward & Lothrop, the department store that has now closed its doors. Lady Bird Johnson and Pat Nixon were among her clients.

After retiring from Woodies in 1973, Via lived on family farms in southern Maryland, where she looked after a few calves, remained active in church, and drove about visiting her grandchildren. But in the late 1980s, as she was approaching her mid-seventies, members of her family began to notice she was getting forgetful. She'd fail to show up when invited to family dinners, she'd sometimes pay the yard man twice, and she'd take more than the prescribed dose of her blood-pressure medicine.

Her grandchildren, Franklin and Theresa, asked her doctor whether she might be suffering from Alzheimer's disease. The doctor had neither a simple diagnostic test nor treatment to offer but told them that the National Institute of Mental Health was studying Alzheimer's and was looking for volunteers.

An initial evaluation at the Clinical Cen-



Michael Selmer volunteered to take a substance aimed at growing new blood vessels to bypass blockages in his heart. Earlier he had survived a heart attack and lost a leg to bad circulation.

ter in 1992 determined that her grandchildren's suspicions were correct and that she would be an excellent candidate for studies by Dr. Trey Sunderland of how Alzheimer's works and whether certain drugs might help.

OVER THE NEXT FIVE YEARS, VIA became one of the most faithful patients in the Clinical Center's Alzheimer's unit, always willing to volunteer for yet another study. "If there is something out there to help me or someone else," she'd say, "I want to do it." She has participated in four lengthy studies involving experimental drug treatments, sometimes receiving the active drug and other times getting a placebo. On 11 other occasions she has come in for cognitive tests, brain scans, spinal taps, and other tests and examinations. In all she has spent about 90 weeks living at the Clinical Center—one stretch lasting six months.

Usually she's there with several other Alzheimer's patients, who are paired off in double rooms but share meals around a big table in a common room that includes comfortable sofas and a television—all behind doors that are locked to prevent patients from wandering. Via brought along several pots of geraniums, which she cared for, but found it difficult to while away the hours until one of the nurses suggested she renew an interest in crocheting. Her first project was an afghan for the Clinical Center's pediatric unit, followed by others for her grandchildren and charities—all in simple but glorious two-color patterns and some large enough to cover a bed.

As her Alzheimer's has progressed, she sometimes forgets and makes too many of the crocheted squares from which the afghans are constructed. But no one who receives one of her works is complaining. And plenty of people have. Not long ago she finished afghan No. 30.

Let a Thousand Studies Bloom

EVERY PATIENT ADMITTED TO THE Clinical Center is enrolled in a scientific study known as a "protocol." These protocols—which must be approved by one of several NIH review boards for their ethics, safety, design, and significance—are the standard methodology of modern biomedical research. While some of these studies are understandable to laymen, others have long, complicated names that are virtually indecipherable.

Protocol # 93-H-0209, for instance, is titled "Development and Assessment of a DDD Pacing Device with Automatic Reverse Hysteresis Atrioventricular Delay for Treatment of Drug-Refractory Symptoms in Obstructive Hypertrophic Cardiomyopathy: Determination of the Molecular Basis for Pacing-Induced Altered Hemodynamic and Electrical Cardiac Behavior." Which, I'm told, has something to do with the heart.

Protocols, which are drawn up by a "principal investigator" and a team of associates, pose a question aimed at pushing closer to a complete understanding of the mechanisms and eventual cure for some disease or disorder.

What causes certain diseases: Is alcoholism related to attention-deficit disorder? Do some migraine headaches have a genetic basis? Can domestic abuse result from panic disorder?

How can diseases best be treated: Do breast-cancer patients have better arm movement if they're given radiation before surgery rather than after? Can thalidomide—the drug that caused hundreds of ghastly birth defects when administered to pregnant women in Europe during the early 1960s—help cure prostate cancer?

There are about 900 studies under way on the Bethesda campus at any moment. The National Cancer Institute, with about 250 protocols, has the most, followed by the National Institute of Mental Health, with about 125. There are wide differences in duration—some protocols lasting just a few months, others stretching back into the 1980s and a few into the 1970s. Between 20 and 50 patients are enrolled in a typical study, though some have as few as 3, and a handful have several hundred. And while many studies offer patients experimental drugs or other treatment, some involve nothing more than tests and observation.

THESE STUDIES COVER DOZENS OF diseases and disorders. Some diseases, while not life-threatening, nag at the quality of their victims' lives—from stuttering and infertility to sleep disorders, short

stature, and anxiety attacks. But others are the much-feared killers of thousands. Cancer, which can arise in many variations and strike any part of the human anatomy, kills about 540,000 Americans each year. AIDS, which is caused by the human immunodeficiency virus codiscovered in the mid-1980s by French scientists and NIH researcher Dr. Robert Gallo, annually kills another 46,000.

To get an idea of the scope of research on the Bethesda campus, flip through a looseleaf binder containing a one-page description of every protocol—a binder that's six inches thick. Some of the diseases have a contemporary ring—chronic-fatigue syndrome, seasonal affective disorder (SAD), attention deficit disorder, post-traumatic-stress disorder. But others—like malaria, rickets, and tuberculosis—are ancient diseases that persist even in the modern world. Some have names most of us have heard—Tourette's disorder, cystic fibrosis, Parkinson's disease, Marfan syndrome, epilepsy, Tay-Sachs disease, sickle-cell anemia, multiple sclerosis—but others are so rare that they are familiar only to doctors and those unfortunate enough to suffer from them.

Many of these rare illnesses, sometimes referred to as "orphan diseases" because they affect so few people, get more attention at NIH than anywhere else in the world. Studies of these diseases often provide clues to curing afflictions that are more common, which is why NIH has some of the leading experts on such things as these:

PANDAS. Short for Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections. After contracting strep throat, children with this disease become obsessive-compulsive and suffer from tics.

Job's syndrome. Like the biblical character whom God tested by afflicting him, victims of this disease suffer from boils on their bodies and are susceptible to infections.

Tangier disease. A genetic lipoprotein deficiency that affects the nervous system. It was discovered by former NIH director Donald Fredrickson among residents of Tangier and other islands of the Chesapeake Bay.

Turner's syndrome. This chromosomal disorder affects girls; patients suffer from short stature and abnormal ovarian development resulting in infertility.

WITH SO MANY DISEASES BEING studied at the Clinical Center, a walk through its lobby and corridors can be a heart-wrenching experience. Some patients are confined to wheelchairs, tap along with canes, or are wearing splints or bandages. Others suffer from stunted growth, obesity, disfiguring skin diseases, or disorders that have left their bodies distorted in ways that provoke strangers either to stare or to turn away.

Treatment too comes at a price—limbs lost to surgery, bodies puffed up by drugs, hair lost to chemotherapy. At the National Cancer Institute, one benefit of volunteering for some studies is a free wig.

The techniques NIH uses to understand and treat these diseases cover the full range of state-of-the-art medicine. High-tech machines—from widely used MRI and CAT-scan units to more exotic PET scanners—provide detailed views of the body's interior to study disease and normal processes alike. One researcher is using such machines to study how the brain functions when people play chess. Other studies test surgical techniques, including one that is trying to discover whether breast-cancer patients do better with radical or nonradical procedures. Still other studies are testing medical devices, one of which is a leg brace for children who suffer from brittle bones caused by a disease called osteogenesis imperfecta.

The techniques NIH uses to understand and treat these diseases cover the full range of state-of-the-art medicine.

The Bethesda campus of NIH also has been a pioneer in gene therapy, the promising new technique that seeks to cure diseases by replacing a patient's faulty genes with corrected copies. In 1990, a team of scientists from the National Cancer Institute and the National Heart, Lung, and Blood Institute—led by Dr. French Anderson, Dr. Michael Blaese, and Dr. Steven Rosenberg—conducted the first gene-therapy trial by inserting a corrected copy of a faulty gene into white blood cells to reverse a four-year-old girl's rare immune deficiency. Rosenberg also has experimented with gene therapy in treating patients with melanoma.

But no treatment at NIH is quite as common as drugs, which are used in an estimated 70 percent of the studies in which some form of treatment is offered. Some of these drugs already are widely used against certain illnesses but are being tried at NIH on different diseases—a drug that is effective on schizophrenia, for instance, is now being tried on obsessive-compulsive disorder.

Other drugs, donated by pharmaceutical companies, are experimental compounds that have passed tests on animals and are now being tried for the first time on humans, first to see if they are safe and at what dosages and then to see if they are effective—the twin standards applied by the Food and Drug Administration before a drug goes on the market.

In all, says George Grimes of the Clinical Center pharmacy, NIH studies are using about 1,750 drugs at the moment, 150 of which are not yet approved for sale.

Growing New Blood Vessels

MIKE SELMER STEPPED OUTSIDE his house in Beltsville, Maryland, at half-time of the 1991 Super Bowl to take a smoke, lighting up as he had for 35 years. When he came inside his wife noticed that he looked pale, and he admitted to a little tightness in his chest, even as he dismissed it as a cold. Sensing that it might be more serious, she insisted on calling his doctor, who told her to call an ambulance. On the way to the emergency room, Selmer suffered a massive heart attack that put him in intensive care for a week and led to the discovery of blockages in the arteries of his heart and to quadruple-bypass surgery.

Selmer, who was 58 at the time and owned a small house-remodeling company, quit smoking after the heart attack. But about six months later he reached under his car seat one day for a rag to wipe his fogged-up windshield, and his hand came to rest on an old unopened pack of cigarettes. "I opened it and lit one up," he remembers. "It was the best high I'd ever had in my life. I felt it from the tip of my toes to the tip of my fingers. The rush was so strong I had to pull to the side of the road."

He took to sneaking smokes—even resorting to walking the dog so he could be alone—despite the warning from doctors that smoking and his lifelong diet of fatty foods had damaged his circulatory system and put him at risk for more trouble. He finally quit again when he began having trouble with his left leg—intense pain and difficulty walking, the discovery of an arterial blockage in his upper leg, replacement of his femoral artery with a plastic tube, repeated blood clots, and eventual amputation below the knee a little more than two years ago. That took a long time to heal, but he eventually was fitted with a prosthesis and returned to playing golf.

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tires off the other guy's car, put it up on blocks, and put all four tires in the guy's locker. He ended up not doing it because that costs money.

Sometimes guys don't always respond so well. Two years ago training camp was dead. It was dull, nothing going on. So there was a defensive lineman—he's not with the team anymore—and he had one of the worst bodies you've ever seen. And he did something to annoy one of our offensive linemen.

Just for fun I took that *Vanity Fair* cover photo of Demi Moore when she was naked and pregnant and I put this guy's head on it with my computer. All the other offensive linemen got a big kick out of it. They wanted me to put it up in the locker room.

But I went to this guy and I asked him, "Are you a good sport?"

And he said, "Yeah, I'm a great sport."

And I said, "This isn't personal, it was just funny, I just chose you at random" (although I really hadn't—the guy had a horrible body). "Would you mind if I put this up?"

He said, "Okay, let's see it."

So I showed it to him. He looked at me and he was about to punch me out. I said, "I'll take that as a no."

Remembering Reggie

The only opponent I've ever been awed by is Reggie White. I had no idea how I was going to block him. Not only was he very quick, but if he had a mind to, he could also pick you up, carry you up to the third deck, put you in a hot-dog bun, and eat you alive.

The end of the road

When I came into the league I may have been the most clueless rookie that's ever been. Then a few years go by and some guys that you came in with are gone and you start to realize that this is a pretty good deal. Then a few more years go by and you begin to really appreciate where you are and the opportunity you've had. A few more years and you cherish every moment.

The last several years I have cherished every moment. I've taken time out before and after every game to just watch my teammates, to see little things that they do in the locker room and out on the field. I'd go out on the field early or stay out late and just take in the scene. Because playing 12 years in the NFL is a blessing beyond anything I deserve. With every guy it's different. But by the end, most of them are thankful for every day.

The thing I'll miss most is game day. You're out there in front of 70,000 people and you're one of the best in the world at what you do and you know it. And you're competing with the best in the world. I'll always strive for ways to duplicate that. □

Last Best Hope

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PATIENTS LIKE MIKE SELMER WHO suffer from clogged blood vessels around the heart normally are treated either by angioplasty or related techniques to clear the blockage or by surgery to bypass it. Several years ago Dr. Ellis Unger and his colleagues at the National Heart, Lung, and Blood Institute began experimenting with a third possibility—using a genetically engineered substance called "basic fibroblast growth factor" to nudge the body into enlarging or creating blood vessels around the heart to circumvent the blockages. Experiments on dogs using the growth factor were so successful that Unger got approval to begin experiments on humans, and last January he placed an ad seeking volunteers in a local newspaper called the *Senior Beacon*.

Selmer, now in his mid-sixties, was sitting around the house one day last January when he ran across Dr. Unger's ad. Intrigued by the idea, he decided to volunteer: "There was a certain amount of danger, but it had worked with animals, so I figured it might help me."

After a thorough physical—another benefit of volunteering at NIH—he was told that the study was designed simply to test the growth factor's safety in humans and that he might receive either the growth factor or nothing more than a placebo. He got his treatment at the Clinical Center last February, and he's had some follow-up monitoring of his eyes to make sure the growth factor does not induce growth of blood vessels in that sensitive area.

It turned out that Selmer did receive the growth factor rather than the placebo, and he is convinced not only that it had no ill effects but that it has made him feel much better, reducing his angina attacks and reliance on nitroglycerine pills. That may be, but rigorous scientific proof of the growth factor's effectiveness awaits a trial with a different group of patients that may get under way next year.

Searching for Volunteers

NIH SCIENTISTS ARE CONSTANTLY looking for volunteers for their studies, working through a variety of channels to drum up enough patients with just the right disease or disorder. A prime source is other doctors, who refer patients with baffling or difficult-to-treat illnesses because they're aware that NIH has expertise to offer. Sometimes this awareness comes from reading articles by NIH researchers in medical journals, hearing their speeches at medical conferences, or receiving a letter from NIH alerting them to a new study. Other times the connection is more personal. A referring physician may be aware of NIH because he or she trained there, knows someone at NIH from medical school, or has referred patients in the past.

Researchers also find patients by developing links with the dozens of national associations, foundations, and patient support groups organized around various diseases. The Foundation for Ichthyosis and Related Skin Types is helping recruit families with these disorders through its newsletter. The National Institute of Allergy and Infectious Diseases has established links with neighborhood clinics in the Washington area to increase the number of African-American patients in certain studies of HIV and AIDS.

THERE ALSO ARE WAYS FOR POTENtial patients to initiate a contact with NIH directly, though a doctor's referral eventually is required of anyone who enrolls in a study or becomes a patient at the Clinical Center. Brief descriptions of studies in every institute are posted on the World Wide Web (click on Current Clinical Research Studies at http://www.cc.nih.gov). Some institutes also run ads in newspapers, and stories on television and in the press often generate an outpouring of recruits. A report on Dr. Ellis Unger's heart study in *USA Today* brought in about 100 new volunteers.

People who are ill—or their doctors—may also call toll-free numbers to get information about studies being conducted on the NIH campus. You may call 888-624-1937 for cancer, 800-772-5464 or 800-243-7644 for AIDS-HIV, and 800-411-1222 for studies of other diseases. Typically about 75 percent of calls come not from doctors but directly from ill people or their relatives.

Some seem desperate. "I remember a gentleman calling who had a lung disorder," says Dottie Cirelli, who runs one of the phone banks. "Treatments hadn't worked, the disease was terminal, and I could hear he was having trouble breathing. Unfortunately, we weren't studying his disease at the time. You try to be helpful in cases like that, perhaps referring someone to some other medical center. But sometimes all you can do is spend time listening."

SOME STUDIES, ESPECIALLY THOSE involving such diseases as cancer and AIDS, are flooded with so many volunteers that enrollment is shut off or waiting lists are established. Far more common, though, are studies that can't find as many subjects

as needed—designed for 20 patients perhaps but with only one enrolled after six months or approved for 250 patients but able to find only 60 after several years.

One difficulty: Patients in other parts of the country sometimes choose to go to academic medical centers closer to home. Ironically, these centers' research may be supported by NIH grants and some of their personnel may have been trained in Bethesda.

The pool of potential patients may also be limited by the nature of the disease itself. Some are so rare that only a handful of people in the entire country are affected, requiring years to accumulate the patients needed to push research forward.

For other diseases, the recruiting pool is limited because they affect only a certain segment of the population—the old, the young, men, women, or a certain racial or ethnic group. One study, for instance, is exploring the reason for high levels of obesity among African-American women. Other researchers are working on Gaucher's disease and Tay-Sachs, which affect mainly Jews.

Even if you have a particular disease, there's a chance that you might be turned down because researchers are looking for volunteers with very specific profiles. They may be looking only for people of a certain height or weight or whose blood pressure is in a given range. Sometimes they're interested only in studying patients suffering from a disease at a certain stage—eliminating those who are already too sick and others who are not sick enough. Other times they specifically exclude people who already have been exposed to certain drugs, so as not to distort the results from experimental drugs under investigation.

NIH IS UNUSUAL IN ANOTHER RESPECT: Certain volunteers are enrolled in studies not because they suffer from illness but because they are healthy. These volunteers are used to understand what is normal in the functioning of the human body and mind; in one study, researchers are observing how people walk to determine what constitutes a "normal gait." Such volunteers are used in dozens of studies, filling out questionnaires, taking psychological tests, working out on exercise machines, giving samples of blood and urine, getting spinal taps, being examined by high-tech scanners. Frequently they are paid a small fee to cover their time and discomfort.

NIH has a registry of about 6,300 healthy volunteers, and last year about 3,500 were asked to participate in everything from studies of sleep disorders to the process of aging. Most are residents of the Washington area who can get to Bethesda easily, some are NIH employees, but others come from afar, including relatives and friends of patients.

Trying to Live Past the Age of 13

TARA LEE SHELLHOUSE WAS JUST short of two when a blood test at the Medical College of Georgia in Augusta determined that she was suffering from a rare illness called chronic granulomatous disease. First recognized and named by researchers in the mid-1960s, CGD is caused by a genetic defect in which certain of a person's white blood cells do not manufacture disease-fighting hydrogen peroxide. That made its young victims so susceptible to infections that their prognosis was an early death.

"They told us horrible stories," remembers Tara's mother, Brenda. "They said she would never be able to go to school in a regular classroom because of the risk of infection and that a lot of kids didn't live past the age of 13."

Other doctors were more optimistic and monitored Tara's illness as she finished high school and even did some modeling. But there were tough times, including two extended hospitalizations at Duke University Hospital when she was 6 and again at 12. Twice she started college but became too ill to continue, and finally she went to work as the office manager of her family's funeral home in Aiken, South Carolina.

Last February she was overtaken by yet another infection, which she could not shake despite a month in the hospital in Augusta. In April she arrived at the Clinical Center in Bethesda—a logical place considering doctors there had experience with about 120 of the 1,100 CGD victims thought to exist in the United States.

Tara, now 24, was in such terrible shape that her father had to lift her from the taxi to a wheelchair to bring her into the Clinical Center. She was suffering from a nocardia infection, and she eventually sank so low that she spent a couple of weeks in the intensive-care unit and was placed on a ventilator. She does not even remember a visit from South Carolina Senator Strom Thurmond, who once owned a home in Aiken built by her father, Robert, and whose son and daughter were her high-school friends.

AMONG THOSE IN CHARGE OF Tara's case was Dr. John Gallin, who serves as the Clinical Center's top administrator in addition to continuing research on CGD and other rare diseases. During more than two decades of work at the National Institute for Allergy and Infectious Diseases, Gallin has been one of the leaders in figuring out the mechanisms of various types of CGD, in isolating the genetic flaws that cause them, and in finding drugs that have reduced infections by 70 percent.

So Gallin and other members of his research team, Dr. Harry Malech and Dr. Steven Holland, had lots of experience in dealing with cases like Tara's. They arranged for doctors at Georgetown University Medical Center to surgically remove some of the infection from her ankles and knees, they gave her normal white cells capable of manufacturing the hydrogen peroxide her own cells could not, and they put her on cotrimoxazole, one of the drugs that had been effective with other other CGD patients.

It worked: Three months after being carried into the Clinical Center she walked out on her own to return to South Carolina. In the long term her hope for a permanent cure may depend on gene therapy, which Gallin and his colleagues already are working to perfect.

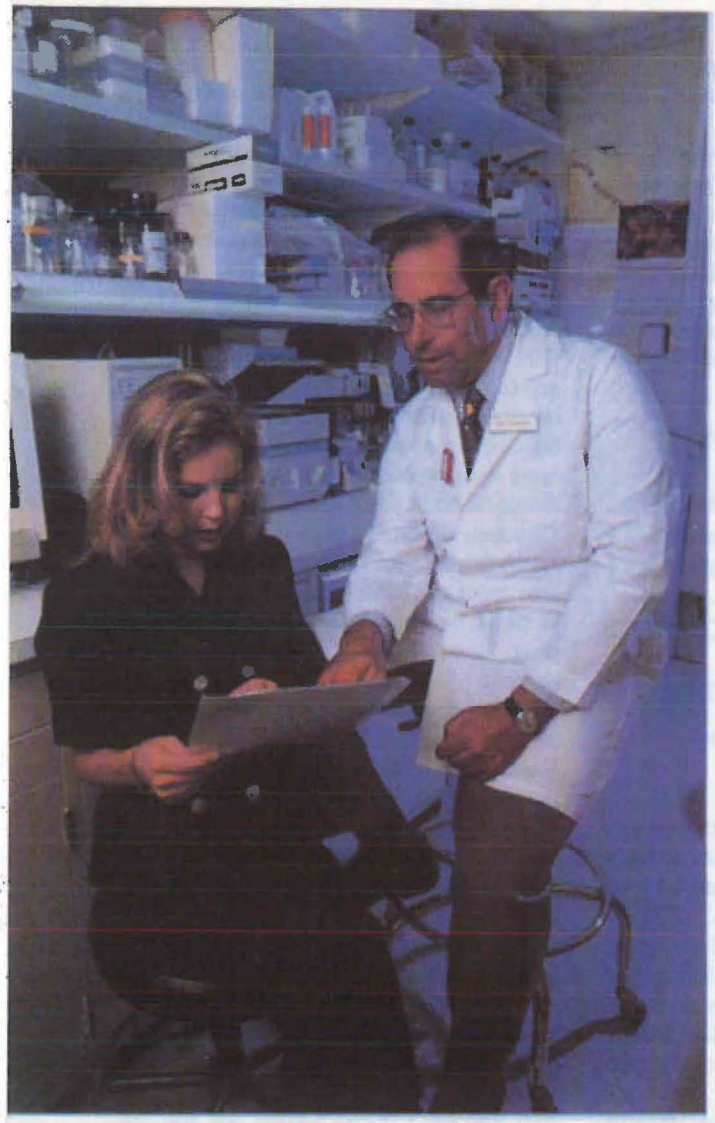
Where There Is a Chance for a Cure

MANY PATIENTS WHO ENROLL IN studies at the Clinical Center have arrived at a point in their illness when all other options seemed to have been exhausted. Often they have spent months or years consulting with a primary-care physician and with hometown specialists, or been examined and treated by doctors at other medical centers. But nothing has worked—the diagnosis is uncertain, no treatment exists, or all the standard treatments have failed—and the doctors have at last said, "If any place in the world can help you it would be NIH."

So NIH becomes a place of last resort: Perhaps here—with all the high-tech equipment, with the concentration and interplay of some of the best minds in medicine, and with access to experimental drugs—there is a chance for a cure.

Another bonus is that all treatment at the

When no treatment exists, or standard treatments have failed, doctors may at last say, "If any place in the world can help you it would be NIH."



Dr. John Gallin is head of the NIH Clinical Center and an expert on chronic granulomatous disease. A recovered patient, Tara Shellhouse, is ready to go home after three months of treatment.

Clinical Center is free. Budgetary pressures have put this tradition under stress—more people these days are treated without expensive inpatient visits, follow-ups of patients don't stretch out as long as they once did, ailments that are not strictly related to a study are left to hometown doctors, and there has been talk higher up in the government of forcing NIH to recoup some of its costs from health-insurance companies.

But free care survives—a godsend not only for the estimated 20 percent of Clinical Center patients without health insurance but also for those whose illnesses have gone on so long that they are bumping up against private insurers' spending caps, face insurers' unwillingness to finance experimental treatments, or have drained their own pockets. Many of the institutes also subsidize travel for patients, with airline tickets purchased at a discounted government rate, mileage reimbursements, and per diem arrangements on hotels and food.

Participation in an NIH study also offers patients something they can't get in a normal hospital—an outlet for their altruism, which seems to grow in many people as their own situation deteriorates. "The information we learn from you may help others who have the same disease, " says a brochure given to new patients, many of whom feel deepest kinship with others in the same straits as themselves.

ARRAYED AGAINST these benefits of coming to NIH are some drawbacks. It may mean frequent trips from far away that require absence from a job, entail expenses not covered by NIH reimbursements, or are physically tiring. Fred Boykin, a Clinical Center social worker, tells of the demands on one of his patients, a man who lives on the West Coast. His treatment required him to make roundtrip flights between his home and Bethesda every week for two months, followed by another two months of trips every other week.

Some studies also require patients to remain in—or close to—the Clinical Center for long periods, leading to isolation from their families, friends, and communities. Although the average stay at the Clinical Center is about nine days, there are patients who stay for weeks or months at a stretch. Some children miss so much school during these stays that NIH has teachers available to coordinate their homework with teachers back home.

Occasionally the homesickness is more than a patient can bear. Dr. John Fletcher, a former Clinical Center bioethicist, tells the story of a woman with lupus who was torn between staying at the Clinical Center during Christmas holidays to undergo a biopsy that was crucial to the research or going home to her family. "She said, 'I feel good for the first time in three years and I want to be at home. And yet I feel an obligation to the physician who is conducting the research.' After discussion with everyone, it was clear that her needs ought to take precedence over the needs of the study. The biopsy was lost, but she went home."

Research subjects also may be exposed to the pain and discomfort that accompany the extra diagnostic procedures and experimental treatments involved in research, including extra blood draws, biopsies, and lumbar punctures. And some experimental drugs—being used in humans for the first time—may have toxic side effects that are not entirely predictable and make patients very ill.

Drug toxicity is carefully monitored, and dosages are adjusted or studies stopped if patients appear in serious danger. Real disasters are rare, but they do occur. In 1993, during a study of an experimental drug for chronic hepatitis B involving 15 patients, 5 of them died suddenly when the drug proved too toxic for their livers. Two others survived only through transplants. That prompted three separate investigations—a critical one by the Food and Drug Administration and others by an NIH advisory panel and the National Academy of Science's Institute of Medicine describing the episode as an unavoidable accident in which the drug's hidden toxicity had not shown up until it was too late.

ETHICAL STANDARDS GOVERNING research on human subjects at NIH are spelled out in federal regulations, which are aimed at avoiding repetition of abuses that have occurred both in this country and abroad. The torture and killing of Jews by Nazi doctors under the guise of medical research prompted prosecutors at the Nuremberg trials to draft one of the world's first ethical codes governing human-subject research in 1949. Exposure in the early 1970s of the US Public Health Service's Tuskegee syphilis experiment, in which poor black men in rural Alabama had been denied effective treatment by penicillin beginning in the 1930s so that doctors could study the progression of their illness, further heightened awareness of ethical issues.

Three ethical principles are paramount in the research done with humans at NIH and any other institution using federal money, says Christine Grady, a Clinical Center bioethicist. The anticipated benefits of all studies—whether to a patient hoping to be cured or to society at large—must justify the risks he faces. Subjects must consent to participate voluntarily after being informed of the procedures and the risks involved, and they must be given the right to withdraw at any time. No group—like the orphans, prisoners, mentally retarded, aged, or poor who once were exploited in medical experiments—is to bear the burden of research risks unduly.

Another decision facing would-be pa-

tients at NIH is whether they wish to participate in studies where they may be given a placebo—essentially a useless compound of milk sugar—instead of the experimental drug whose safety and effectiveness are under study. Typically the subjects in such studies are randomly assigned to two groups—one that gets the active drug and one that gets the placebo—so scientists can determine whether taking the drug really is better than doing nothing. Frequently these studies are "double blinded," meaning that neither patients nor researchers are told who's getting what. This keeps results from being distorted by wishful thinking.

Records of who's getting the placebo and who's getting the active drug are kept in the Clinical Center's pharmacy department, which prepares and dispenses look-alike pills or intravenous bags for both groups. Among the wonders of the pharmacy is a placebo-making machine that can turn out pink capsules at the rate of one per second as well as row upon row of shelves lined with dozens of drugs labeled in code. The codes display a certain whimsy, using names like Zebra, Wren, and Finch. "We like to lighten up once in a while," explains one pharmacist.

Studies using placebo control groups present potential subjects with a dilemma. On one hand: It's possible you could take an injection or pill every day for weeks, months, or years that was nothing more than saline solution or milk sugar. On the other: Since no other treatment is usually available, you at least have a 50 percent chance of getting an otherwise unobtainable experimental drug that has at least some chance of being effective. In rare instances, the uncertainty is more than patients can bear; they take their capsules to a lab for analysis and drop out of studies if they're getting a placebo.

Most researchers insist that placebos are necessary to ensure scientific rigor, but policies have been developed that allow people who get the placebo to switch to the active drug if it quickly proves effective. Some studies have independent review committees, which are given special access to preliminary results and have the power to stop or "unmask" a blinded study if a drug is showing great results. That's followed by a "clinical alert" to spread the good news to practitioners throughout the country. Since 1990, more than a dozen studies funded by NIH throughout the country have been halted early and clinical alerts issued, involving improved treatments for breast cancer, sickle-cell anemia, rectal cancer, heart disease, pediatric AIDS, and several other diseases.

Mitch Brean of San Diego, who's been HIV-positive for ten years, has responded well to an experimental drug. The NIH pharmacy dispenses about 1,750 drugs.

Battling the AIDS Virus

IN 1987, AS FEAR OF AIDS WAS growing among gay men throughout the country, Mitchell Brean was living in Los Angeles, where he had just started a small company to manufacture high-end furniture for the interior-design trade. He was the picture of health, just 29 years old, but news that a former partner had died of the disease was enough to convince him to go in for a test. He was HIV-positive.

Brean started taking the new antiviral AZT, a drug whose effectiveness against AIDS had been established in large part by the work of scientists at NIH. But AZT was new then, and he quit after three months because it was uncertain whether it ought to be taken as soon as possible or delayed until his health began to deteriorate.

A couple of years later, in 1989, Brean moved down the coast to his hometown of San Diego. His business prospered and his health remained good. "I took good care of myself—exercised, took vitamins, was careful about what I ate," he says. "And I'd never been a drinker or smoker." While people are not considered to have full-blown AIDS unless their T-cell count drops below 200, his count was nearly 1,000.

But a couple of years ago his T-cell count began to decline to a worrisome level—around 500—adding some urgency to his reading of AIDS-treatment newsletters and the medical items in a local gay newspaper. One day he happened on to an article about a doctor in San Diego who was enthusiastic about an experimental drug called interleuken-2. Brean made an appointment to see him.

The doctor explained that IL-2 was very expensive—an experimental therapy his insurance company was unlikely to pay for—but that he might get it free if he qualified for a clinical trial under way at NIH in Bethesda. Brean called the number the doctor gave him and was put on a waiting list.

A YEAR LATER, IN APRIL OF 1996, Brean got a call asking if he would fly to Washington—the first trip was at his own expense—to see if he was a fit subject for one of several IL-2 studies. Doctors explained that he'd be getting IL-2 intravenously in combination with other drugs, including a much-touted protease inhibitor. They talked about the side effects—"think of the worst flu you've ever had, then multiply it by ten"—and they drew blood to make sure his T-cell count was below the cutoff point of 500.

In California he had tested in the 400s, so he was confident he'd qualify, but a few days later came a call that his count at NIH was 575. Luckily there was a similar study—this one testing delivery of IL-2 in a more convenient injection form—that would accept him.

For a year Brean flew every other month from San Diego to Bethesda and took IL-2

and the other drugs for five days under the direction of a study team headed by Dr. Richard Davey of the National Institute of Allergy and Infectious Diseases. The researchers hadn't exaggerated the debilitating side effects of the drug regimen—fatigue, aching muscles, pain in the joints, dry skin, water retention, and high fever. But it was a price that so far has had a big payoff. Brean's T-cell count has risen into the 1,500 range, and the level of HIV in his blood is too low to detect.

Helping Kids Smile

THE MOST INVITING BUILDING ON the NIH campus is the Children's Inn, a wood-and-stone structure that sits amid a grove of old trees just down the hill from the Clinical Center. Outside—not far from a basketball court, playground, and patio—sits the inn's green van, nicknamed the "Looney" because it is covered with paintings of Bugs Bunny, Daffy Duck, Tweety, and other cartoon characters. The skylit atrium inside the inn rises two-and-a-half stories high, with a circular fireplace in the middle, and is filled with gigantic stuffed pandas, frogs, and bears as well as a fish tank and toy train.

The inn has private rooms to accommodate 36 out-of-town families—either for a day or two or for weeks at a time. It's all free, though a donation of between $10 and $50 a night is suggested. Jason Shaft and his mother have stayed here so often that Jason has become a favorite pool partner of Gil Brown, the inn's executive director, and has been given the task of checking out games in the computer room to make sure they are appropriate for younger kids.

The inn, which opened in 1990, was created as a public-private partnership. NIH donated the land, and the $3.7 million construction cost was paid for by Merck & Co., the big pharmaceutical company, whose CEO at the time, Dr. Roy Vagelos, started his career at NIH. It operates on private donations and thousands of hours of time contributed by 275 volunteers, who perform duties similar to those of a hotel staff. Sometimes these duties are extraordinary—a family from a rural part of Mexico, whose daughter had come to NIH for a bone-marrow transplant, had to be shown how to operate the electric lights, running water, and indoor plumbing.

Dr. Philip Pizzo, former chief of pediatrics at the National Cancer Institute, was one of the inn's main founders, but it also has become one of the hottest charities in Washington. Its board members include several congressional wives—Debbie Dingell, Chris Downey, Carmala Walgren, Jane Gephardt, and Marianne Gingrich—as well as ABC's Cokie Roberts. The involvement of Walgren—whose husband, Doug, served seven terms as a Democratic congressman from Pennsylvania until his defeat in 1990—was quite personal. While visiting her teenage babysitter, who was being treated for cancer at the Clinical Center, she became distressed that so many families had no choice but to stay in impersonal hotel rooms. The babysitter, a high-school sophomore from Alexandria named Ginny Cavender, was cured; she's now 26 and teaches at an elementary school in Great Falls. Walgren also once raised a ruckus on the Hill to gain restoration of the right of families to use a Clinical Center WATS line during off-peak hours.

At the Children's Inn, the color scheme is carefully chosen—avoiding red (associated with blood) and yellow (associated with chemotherapy).

THE INN PROVIDES PSYCHOLOGICAL support that no hotel can match. It's designed to encourage children and their families to overcome their isolation by interacting with others who are battling illnesses too. All televisions are in common areas, there are two big kitchens where families share cooking duties, and there is a room for Ping-Pong and pool, a computer center, a playroom filled with toys, and a library.

There's also a party every holiday, including a costume show at Halloween. It once featured a teenage cancer patient from Connecticut named Lizzie Schwanfelder who displayed the kind of wit and spirit that always amazes and inspires members of the Children's Inn staff. All of Lizzie's hair had fallen out as a result of chemotherapy, so she painted her bald head orange and entertained the younger kids as a jack-o'-lantern. When she died in 1993 at the age of 18, her mother, Kathy, became a member of the inn's board.

The inn is intended as a homey retreat from the often scary and painful rigors of treatment at the Clinical Center. Just over half of the kids who stay at the inn have cancer or HIV-AIDS, and they are often weary of the hospital's humming machines, the tubes filled with powerful drugs that make them sick, and the pricks and pokes of doctors and nurses.

The inn's atmosphere is quite different. Doctors are not allowed to enter the premises except in a rare emergency, no one is allowed to wear a white coat, and even the color scheme is carefully chosen—avoiding red (associated with blood) and yellow (associated with chemotherapy).

ADULT PATIENTS FACE A HOST OF problems too, and the Clinical Center tries to help with a staff of nurses, social workers, spiritual ministers, counselors, and an ombudsman. Some patients have financial worries—overdue rent, job insecurity, lack of health insurance, unpaid medical bills. And disease itself generates powerful emotions that are difficult to deal with—shock, disbelief, anger, helplessness, fear, anxiety, and depression.

"One minute your life is okay and the next it's blown apart," says Eileen Dominick, a Clinical Center social worker. "There's a lot of anger and a sense that it isn't fair that you have a life-threatening disease and are sick as a dog." Sometimes nothing can be done except prepare a patient and family to deal with death. "There's a lot of sadness and grief, a lot of giving up what used to be, a lot of trying to find some meaning in whatever time you have left."

One bit of comfort comes from meeting other patients with the same illness—giving rise to an awareness that you are not so terribly alone. This is especially helpful for patients with rare diseases, who may never have met anyone else with their affliction before coming to Bethesda.

Tara Lee Shellhouse, the 24-year-old woman from South Carolina with chronic granulomatous disease, spent three months at the Clinical Center earlier this year on a ward with several other CGD patients about her own age. The trembling she experienced while receiving antibiotics had prompted doctors elsewhere to suggest that she see a psychologist, but her talks with the other patients reassured her: "Gregory gets the shakes, and so does Bryan. I'm not the only one."

Some contacts between patients are more formal, often in support groups organized by social workers. They also arrange telephone contacts between patients with rare diseases, who often are scattered far and wide. And there's a pilot project under way using computer chat rooms to bring together adolescent boys with HIV, who suffer from intense isolation.

Two Things Every Little Girl Wants

WHEN ROXANNE AND DENNIS RUSsell were married four years ago in the Mississippi town of Louisville, they took it

Roxanne and Dennis Russell haven't been able to have a baby because her immune system attacked her ovaries. She hopes NIH has a solution.

for granted that someday they'd begin having children. Roxanne wanted to be a schoolteacher—she now teaches fifth-graders—but she had no doubts she wanted kids of her own: "There are two things that every little girl always wants. And that's to get married and have children. When I was little I used to prance around with a pretend veil and doll babies."

Roxanne and Dennis planned to wait a couple of years before trying to have a child, until she'd graduated from Mississippi State, got her career going, and until some of the illnesses she had experienced seemed under control. She had a thyroid condition call Hashimoto's disease. She also had never established a regular menstrual cycle and experienced hot flashes and night sweats almost as if she were undergoing premature menopause. Despite this, a doctor she was seeing in Birmingham assured her she should be able to have children.

When all attempts were unsuccessful, a doctor in Mississippi decided in 1995 to do an ovarian biopsy and discovered that her ovaries were abnormally small. He told her husband that it would be impossible for her to get pregnant—news the young man finally delivered to her when they got home from the hospital that night.

"I was hysterical," she remembers. "I just couldn't believe it. I just fell over in Dennis's arms and cried. It was the worst feeling in the world. It's so hard to know that you will never have anything that looks like you and talks like you."

IT APPEARED FROM THE BIOPSY that her body's immune system had attacked Roxanne's own ovaries and that nothing could be done to restore fertility. Still searching for a solution, she went to another specialist at the University of Mississippi Medical Center in Jackson. In February of last year, the doctor there put her on hormone-replacement therapy for 40 days, but it appeared to have no effect, and she and Dennis began talking about adoption. Four months later, after noticing what she thought was the onset of a period, she went to a local doctor and was found to be pregnant. She was euphoric, but that ended just three days later when she suffered a miscarriage.

After grieving over the miscarriage for several months, Roxanne decided to follow up on a contact given her earlier by the doctor in Jackson. He had received a letter indicating that a doctor at the National Institute of Child Health and Human Development in Bethesda was looking for women whose ovarian failure was due to autoimmune attacks. The researcher was Dr. Lawrence Nelson, and his study was intended to determine how common the problem is and whether, in a placebo-controlled trial, the drug prednisone might restore fertility.

Roxanne, who is now 25, and Dennis made their first trip to Bethesda in July for an evaluation, and she was accepted as one of the study's first participants. "I don't really have anything to lose," she says. "Even if it doesn't help me, maybe it will help somebody else. That's why I'm honored to take part."

Believing in Miracles

THOUGH MANY OF THE MEDICAL advances made possible by NIH money have occurred in research centers scattered throughout the country, there have been plenty of breakthroughs attributable to work done on the home campus in Bethesda. Decade by decade, here are just a few:

The 1950s: A cure for a cancer of the placenta called choriocarcinoma—the first successful treatment for a malignancy; development of an artificial mitral valve for heart-disease patients; discovery that low levels of fluoride in drinking water could prevent tooth decay.

The 1960s: Development of the first licensed rubella vaccine; discovery of an effective combination drug therapy for Hodgkin's lymphoma; discovery that tooth decay is caused by bacteria; discovery of the mechanisms that regulate noradrenaline, an important neurotransmitter in the brain, which led to the development of better drugs for treating mental disorders.

The 1970s: Effective treatment for childhood leukemia; groundwork for home pregnancy tests; tests proving that lithium is an effective treatment for manic-depressive illness; research establishing the cancer risks of asbestos, smoking, and smokeless tobacco.

The 1980s: Codiscovery of HIV, leading to a practical test to detect infected blood; a powerful new vaccine against *Hemophilus influenzae* type b, a bacteria that caused meningitis in children, which often led to blindness, deafness, mental retardation, and other problems; experiments with AZT, the first antiviral drug to demonstrate effectiveness against AIDS; successful use of an antiviral drug against oral and genital herpes; increased understanding of brain function by measuring its utilization of glucose; treatment for a formerly fatal blood vessel disease known as Wegener's granulomatosis.

The 1990s: An effective treatment for Gaucher's disease, which affects a certain segment of the Jewish population; the first infusion of genetically corrected cells in humans, in an effort to treat adenosine deaminase deficiency, a rare genetic disease that cripples the immune system; new treatments for epilepsy; a new drug that relieves symptoms of Parkinson's disease for some patients; effective drug treatment for

a rare genetic disease called nephropathic cystinosis, which affects the liver and eyes of children; improved treatment for CMV retinitis, a potentially blinding eye disease that affects a quarter of people with AIDS.

SUCH ADVANCES TRANSLATE INTO thousands of people who now survive diseases once considered deadly. Consider the impact of NIH on a couple of young people who were diagnosed with a fast-growing cancer:

Craig Kline, who grew up in the New Jersey suburbs of New York City, was entering his last year of law school at the University of Virginia in 1993 when he began having pains in his abdomen. They were bad enough to send him to the university's hospital, where a CAT scan revealed a tumor that was soon diagnosed as Burkitt's lymphoma. The doctors told him they cured about 35 percent of cases like his but that he might get better results from an aggressive treatment being used at the National Cancer Institute in Bethesda.

At NCI, Kline was enrolled in a protocol directed by Dr. Ian Magrath, an Englishman who had first worked on Burkitt's in central Africa, where it had been identified in the 1950s. Since arriving at NCI in the mid-1970s, Dr. Magrath had been a pioneer in pushing survival rates for this type of lymphoma from 20 percent in the 1960s to about 90 percent, treating it with a chemotherapy regimen combining seven different drugs.

Kline stayed in Bethesda for five months, struggling with side effects that left him 50 pounds lighter and confined to a wheelchair. "It was living hell," he remembers, but the cancer disappeared.

He then put on weight, regained his ability to walk, and passed safely through the six to ten months when all known recurrences of Burkitt's have struck. A year after his initial diagnosis he was back finishing law school at UVa, where he organized a support group for young adults with cancer.

Today, at age 28 and four years removed from his treatment at NCI, he works in a law firm in New York and is active in the Cure for Lymphoma Foundation, which raises money for research.

Last fall, when eight-year-old Nathan Chestnut of Mechanicsburg, Pennsylvania, became lethargic, quit eating, and complained of bellyaches, his mother took him to the family pediatrician. The doctor, feeling a swelling in Nathan's abdomen, ordered an ultrasound test, which discovered what was thought to be an abnormally enlarged appendix that required surgery.

After three hours in surgery, a doctor came out to the waiting room, told Nathan's mother to sit down for some bad news, and reported the discovery of a tumor thought to be malignant. The diagnosis was Burkitt's lymphoma, which is so aggressive that it can double in size in two or three days. The doctor recommended that Nathan be taken immediately to the National Cancer Institute.

The boy was transported by ambulance to Bethesda the next day and put into the intensive-care unit at the Clinical Center. After a couple of days of tests, Dr. Magrath began giving Nathan the same chemotherapy he'd administered to Craig Kline. Nathan stayed in Bethesda for about two-and-a-half months, miserably sick from the chemotherapy, which caused sores in his mouth and hair loss.

For every breakthrough there are lines of inquiry that run into blind alleys, patients who return home without relief, scientists who must rethink their approach. The process may take years—a time when hope and disappointment coexist.

But he left cancer-free and has had good checkups since—well past the danger point for any recurrence. This fall, having gained weight and with his hair grown back, Nathan is heading to school for the fourth grade.

This is not to say that NIH offers miracle cures to everyone. Plenty of the diseases studied there remain unconquered. Some are so little understood that scientists can do no more than follow their natural course, trying to replace their bafflement with the light of understanding. Others are treated with drugs that seem worth a try but eventually prove too toxic or have little effect.

It's an old story in medical science: For every breakthrough there are other lines of inquiry that run into blind alleys, patients who return home without relief, and scientists who must rethink their approach and try something else. It's a process that may take many years—a time when hope and disappointment coexist.

ONE PATIENT WHO FACES AN UNcertain prognosis is Jason Shaft, the 15-year-old boy from Kentucky with neurofibromatosis, who has come back to NIH with his mother, Linda, to see if the drug he's been given has begun to shrink his life-threatening tumors.

Leaving the Children's Inn, mother and son make their way up the hill to the Clinical Center, where Jason has a mid-morning appointment to be scanned by an MRI machine. For four-and-a-half hours he lies inside the confining machine, absolutely still, listening only to the instructions of an attendant and the noise of the scanner as it creates images of the tumors that press against his spine, lungs, and other organs. Just outside the scanning room, his mother passes the time reading magazines—wondering again, as she has dozens of times since Jason was a baby, whether the news will be good or bad.

When the scan is finished, about three o'clock, Jason and Linda go up to a lounge on the 13th floor to wait for news from Dr. Peter Adamson, the physician in charge of the study Jason's enrolled in. Adamson is consulting with neuroradiologists about what the images show, but Jason has so many tumors that it is taking a long time to measure whether they've responded to the drug or not. Dr. Stephane Barrette, a young doctor who's also following the case, passes word to Linda and Jason that they might want to go back to the inn and talk with Dr. Adamson in the morning.

No chance. Linda is too anxious. They'll wait.

"Okay," says Dr. Barrette, "but you know it will be a while."

The clinic is closing as Dr. Barrette exits, leaving Jason and Linda alone. Before long the cleaning people begin their end-of-the-day rounds, dusting the tables, sweeping the floor, and wiping the glass on the aquarium, where a little shark swims back and forth.

About 5:30 Dr. Barrette returns to say that Dr. Adamson wants to meet with the two of them at 11 the next morning.

This sets off Linda's alarm: "Is this something I should stay awake and worry about?"

"No, no, I don't think so," says Barrette.

Just then Adamson himself comes into the lounge and Linda Shaft approaches him with the same question. Putting his hand on her shoulder, he quietly delivers news that is not as good as she'd hoped but will have to sustain her until Jason's next exam: "There's no shrinkage yet, but there's no growth either." □