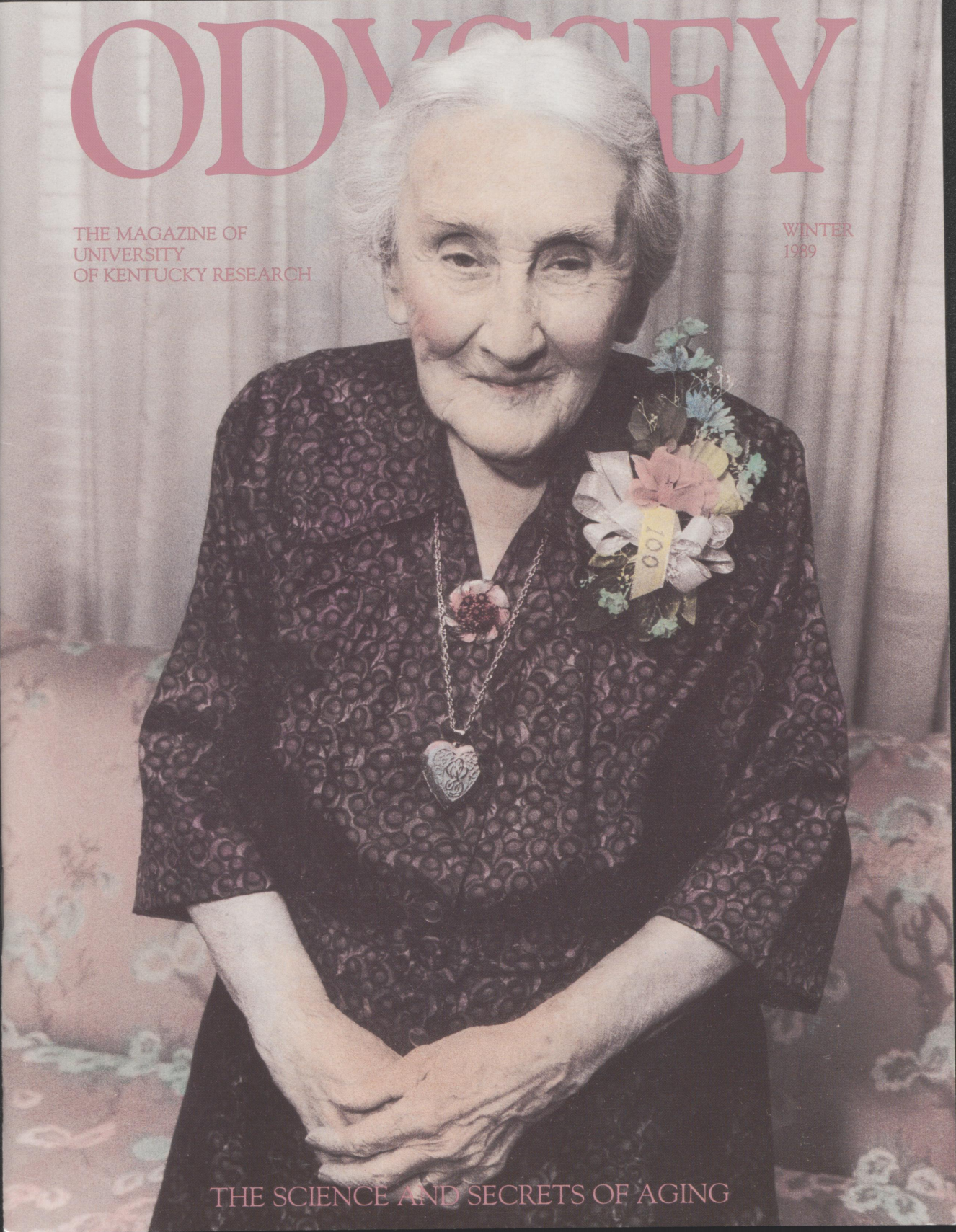


ODYSSEY



THE MAGAZINE OF
UNIVERSITY
OF KENTUCKY RESEARCH

WINTER
1989

THE SCIENCE AND SECRETS OF AGING



The University of Kentucky, the Commonwealth's graduate education and research institution, exists to provide opportunities for the education, personal growth and development of individuals and to contribute to the improvement of society.

With this mission as its premise, one goal of the University is to conduct programs of basic and applied research which support graduate and professional education, provide for the advancement of knowledge, and seek solutions to the acute problems of society.

The University's research mission also acts as a magnet for attracting top graduate students who want to participate in nationally competitive research projects. This research experience can offer them a significant advantage in their education while laying the foundation for future research and development. ODYSSEY Magazine, through articles about various research projects and graduate education programs, reflects the breadth of the University's search for new knowledge and the myriad of research endeavors underway. The progress that the University has made toward achieving its research mission and securing the extramural funds required to support these types of endeavors would have been impossible without the talents and dedication of our researchers.

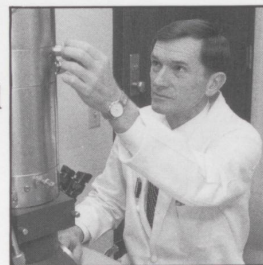
The goal of ODYSSEY Magazine is to offer the reader the opportunity to share in some of the excitement, curiosity and creativity evident in the research underway at the University of Kentucky.



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ODYSSEY is a magazine published by the Office of the Vice President for Research and Graduate Studies. Each issue of ODYSSEY describes only a few of the many University of Kentucky research projects underway in a variety of areas.

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Cover: Lucy Powell, one of over 500 Kentucky centenarians who have taken part in a University of Kentucky study of the state's oldest old.



**LIVING A HUNDRED YEARS:
GENETICS, PHYSIOLOGY,
OUTLOOK AND OTHER SECRETS**

by Jeff Worley

Dr. David Wekstein, associate director for the Sanders-Brown Center on Aging, remembers the day when the invited speaker, a white-haired woman named Mary Cross, presented a lecture to first-year medical students at the University of Kentucky. After she had stood in front of them for an hour, she asked if there were any questions. "How is your health?" asked a student in the second row. Mrs. Cross, age 101, looked directly at the young man, reached over without bending her knees and put the palms of her hands flat on the ground. "One final note for all of you to take with you," she said from her new position—"when you graduate, don't you overcharge. It's the wrong thing to do!"

The oldest old have always fascinated and intrigued us. They are a tangible link to a far-away past we can only vaguely imagine. They are a living history: one centenarian describes the severe, determined face of Carrie Nation as she marched into the town's only saloon; another recalls watching the portly Grover Cleveland strolling on the White House lawn; and another clearly remembers, on December 31, 1899, listening to her father's clock on the mantel tick into the new century.

Partly because so little was known about this special group, Wekstein, a professor of physiology and biophysics, is now involved in a study of Kentucky centenarians, a project that seemed to grow naturally from an earlier idea to recognize and honor 100-year-olds living in Kentucky. "This current project resulted from our idea of sending certificates to centenarians throughout the state. We started doing this about five or six years ago through the governor's office and the president's office here. We've sent one to every name reported to us—about 500 so far," Wekstein says.

As new names came into his office, and more and more certificates left in the mail, Wekstein realized the potential for a fascinating project. "I thought, 'Why don't we pull together people from various parts of the university, look at this unique group, and see what we can learn from them.'" Wekstein says that in the beginning the focus of the project was to describe a phenomenon, not to attempt to answer any questions. "There was so little information available about people of this age, we wanted, first, to describe them



David Wekstein

“One centenarian in Western Kentucky told me that when she dies she wants her body to go to a university for research—and that her 104-year-old brother feels just the same way. How many people have a 104-year-old brother!”

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accurately. Our goal was simply to find out what 100-year-olds in Kentucky had in common."

Funded by the Sanders-Brown Center and two private sources, the Beverly Foundation and the Andrus Foundation, the centenarian project was initiated in 1984 by a time-consuming, but necessary, first step. With a listing of the telephone numbers of those who had made referrals, Wekstein and research associate Ms. Charli Kirkpatrick began to interview this group to find out how functional the centenarian was. Those who were characterized as "quite functional" were contacted in person. If the researchers were satisfied that the centenarian was mentally competent, they described the project and asked him to participate. All participants had to then sign an "informed consent" document.

At this point the researchers got a wide range of responses. "Quite a few were happy to participate, pleased to be asked," says Wekstein. "But there were some that wanted no part of it. One man in Louisville—we'd been warned by his niece that he was 'mean and nasty'—said he was too involved with his stocks and bonds portfolio. Another hundred-year-old, who had just come home from getting his driver's license renewed, said it would interfere with his social life!"

Persons 85 years of age and over now constitute the most rapidly growing segment of the population.

The next step for Wekstein and Kirkpatrick involved a bit of detective work—verifying the age of the centenarians. Since Kentucky didn't keep any birth certificates before 1917, no one born before that date can prove date of birth. The investigators, therefore, turned their attention to census data, knowing that after 70 years this information is part of the public record. "We'd go back to the 1900 census, for example, to see if the person was 11 or 12 then," Wekstein says.

"If we found that age reported in 1900, we were satisfied, since there's no reason to believe that anybody at age 12 would exagger-

ate how old she was. It's a perfectly acceptable way of verifying age." The oldest participants in the study have been 106.

So far, the researchers have interviewed over 500 centenarians, over 40 of whom have participated in in-depth, personal interviews and clinical work. "We have done a great deal of clinical chemistry with this group," Wekstein says, "as well as CAT scans and cardiovascular work to get some fundamental kinds of information." One of the problems the researchers are focusing on is dementia, loss of intellectual function, in the older population.

"We know that thirty percent or more of the population 85 and older have Alzheimer's—some studies say up to two-thirds of this group—so you could predict that in the centenarian population most of them would be demented, which is not the case," says Wekstein. "In our group, in fact, only about 40 percent were demented." He cautions that this is not a study of every centenarian in Kentucky: "These people were all self-reported in some fashion, so if someone is demented and living alone or no one cares about him, we wouldn't know he exists. So the study is skewed in that way."

There are no accurate numbers to tell us how many centenarians live in the United States, though Wekstein estimates that one of 10,000 people are 100 or older. Of Kentucky's 3.5 million people, then, there would be 300 to 400 centenarians at any one time. Wekstein says that although the study doesn't include all of them, 70–80 percent are contacted. "From one perspective," Wekstein says, "that's not at all problematical. In almost any study of a group, you want to exclude those who are sick. We are interested in looking at only healthy centenarians."

What traits do these centenarians share? One common characteristic among the group is a reported history of longevity in the immediate family. The centenarians' mothers and fathers lived well beyond the time their peers

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Lucy Powell: Mackville's Oldest Citizen



Lucy Powell

When we arrived at the Medco Center of Springfield, Kentucky on a windy day in November, Mrs. Violet Elliott, Medco Administrator, assured us that Lucy Powell was looking forward to the visit.

"There's just one thing," Elliott said. "Lucy wanted me to let you know that she can't chat past 4:00. Friday's her bingo day."

I had driven from Lexington along the Bluegrass Parkway, the wind picking the maples and hickories bare, with Lisa Burgess, senior research assistant at the Sanders-Brown Center, and Mark Zerof, a photographer who accompanied us. We had come to see Mrs. Lucy Powell, one of over 500 Kentucky centenarians participating in a University of Kentucky study of the state's oldest citizens.

Mrs. Powell—Lucy—was clearly delighted to see us, and seemed especially pleased to see the two cameras Mark carried over his shoulders. "Now don't you take my picture when my mouth's open," she warned Mark after we had been introduced to her by Lisa, "the last one that did

that made me look like an old fish!"

And before any photos could be taken, Lucy wanted to pin on the corsage she received on her 100th birthday in 1987. In the middle of the flower arrangement was a blue ribbon showcasing the number 100 in gold script.

Lucy was born on the family farm about five miles outside of Mackville, Kentucky where she was raised with her brothers, Carter and Charlie, and a sister, Sarah Elizabeth. She attended school from the time she was six until age 13. Although her schooling was brief, one memory stands out.

"I remember being punished at the old White Oak Schoolhouse," Lucy said. "The teacher kept me in during recess and wouldn't let me have nothing to eat."

"What had you done that was so bad?" I asked.

"I bit a girl, right on the wrist."

Asked why she'd done this, Lucy replied, "Meanness probably."

Lucy added that later in the schoolday the girl sitting next to her gave her a piece of cake from her desk. "Oh, they loved me, really. I

was a little bitty fella . . . they just loved me."

At age 27 Lucy married Will Powell. They lived on a 212-acre farm in the Mackville area and raised crops and livestock. Will, with hired help, would tend the tobacco and corn crops and Lucy cooked for everyone. She never smoked any of the tobacco herself, but did admit to one short-lived "terrible bad habit"—drinking coffee.

"I didn't drink coffee when I married Will, but he wanted his coffee three times a day—breakfast, dinner, and supper. I got tired of making it that long. I got to pouring a little on a saucer and then into a teacup. But it didn't agree with me so I quit."

When Lucy talked about their life together on the farm, her words seemed lighter, even more sure of themselves. "We had big times, good times," she said. "We didn't have any children, but I had lots of pets. My favorite was Buster, my pet pig. I could hold him in my arms at first, but then he got big—over 300 pounds."

After her husband died in 1958, Lucy remained on the farm for ten years before moving into a home in Mackville. In the 1970s, she broke her hip and her freedom was restricted, but she didn't let her accident slow her down. Instead, she took up the art of quilt making and found she was extremely good at it.

"I pieced 25 quilts and quilted them," she said, "and I've sold every one." She had planned to keep the last one, but a man who had already purchased one was so insistent, she sold the last one to him too.

On her 100th birthday, Lucy was named a Kentucky Colonel and received correspondence from President Reagan and Governor Martha Layne Collins. "I got all kinds of presents," Mrs. Powell told us, "over 230 cards and letters."

But now she was suddenly distracted—perhaps, I thought, by another memory she wanted to share with us. She was looking beyond me to the opposite wall. It was 3:45, time for us to shake her hand and be on our way.

Jeff Worley

lived, and had brothers and sisters who also fit this pattern. "One centenarian in Western Kentucky," Wekstein says, "told me that when she dies she wants her body to go to a university for research—and that her 104-year-old brother feels just the same way. How many people have a 104-year-old brother!"

The second commonality is that the members of this select group have lived a lifestyle that is consistent with longevity. None has had any significant history of smoking (though two were tobacco chewers), they were not heavy drinkers (though some occasionally took something for "medicinal purposes"), none was obese (defined by Wekstein as ten percent above ideal weight), they drank very little caffeine, and most weren't red-meat eaters.

"I won't say they read the book and knew what to do," says Wekstein, "but they pretty much stayed within the American Cancer

Society guidelines. That's basically how these people have lived."

Another important shared attribute is that these centenarians are very future-oriented. One of the men in the study who is 102 years old is writing his autobiography. He is currently up to the time (1916) when he was thirty. He has every intention, Wekstein says, of finishing it. "All of these centenarians had definite plans for the months ahead. They weren't just sitting around waiting to die."

Although these findings weren't particularly surprising, Wekstein says that they are valuable because now some hard data have been gathered to support them. There have been, though, a number of surprises. "I was amazed, for one thing, how easy it was to identify these people. I never in my wildest imagination thought that we would have hundreds of them. A second surprise for us was the number not living in long-term facilities. We

Lisa Burgess, senior research assistant at the Sanders-Brown Center, and Sumner Davis, a participant in the UK centenarian project. Davis, 103, lives with his daughter Jane Davis.



envisioned the vast majority to be in institutions and that wasn't the case for about half of them."

Although the immune systems of the centenarians had "gone downhill about the way we expected," he thought that there would be a much higher percentage that were demented by this age. "In terms of CAT scanning of the brain, they most certainly did lose brain tissue as they grew older. But they didn't lose it at the rate we would have predicted. They didn't seem to lose themselves as quickly as the rest of their peer population. So although they weren't immunologically spared, the loss of brain tissue didn't go downhill that way," Wekstein says.

Charli Kirkpatrick, who conducted all of the telephone interviews during the project's first two years, emphasizes the importance of the data that have been gathered, and adds that the project was "intensely interesting." "It's the closest thing I ever did to not working," says Kirkpatrick, now the coordinator of the Memory Disorders Clinic at the Sanders-Brown Center. "There were very few people I didn't fall in love with. And even though I have a new position, I've been in contact in the last month with the four of the 38 people still alive that I interviewed four years ago. I'm still trying to find out if another three are living."

Ms. Lisa Burgess, the project's current research assistant, thinks of the job as an important step in gathering information, but she also thinks of it as an opportunity to hear a wide variety of "life stories." "These people are very important historically—they've witnessed incredible changes in their lives. Listening to them is a wonderful way to learn about Kentucky's past."

Burgess, who has interviewed over 220 centenarians during the past year, is continually surprised how many of them are alert and physically capable of living on their own with a minimum of care from others. "One thing the study has done is to break the stereotype of the totally befuddled, bedridden 100-year-old," says Burgess. "Only 18 percent of those I've interviewed fit that pattern."

The centenarian study, Wekstein mentions, has been funded in a number of ways. "We've been lucky enough to get money from here

“ One thing the study has done is to break the stereotype of the totally befuddled, bedridden 100-year-old. ”

and there to keep the project going," he says, and now the plan is to put together a grant application for a "well-funded, five-year study." Major funding would allow the researchers to test some hypotheses based on information that has been gathered.

"One thing we'd like to do is a prospective study," Wekstein says. "If we could find people, say, in their 50s whose parents lived to a rightful old age, and the people in their 50s had a lifestyle similar to that of their parents, we could study the sons and daughters over time to determine a correlation."

Wekstein has already collected a pool of close to 5000 research volunteers, all over 60 years of age, in Fayette County. He currently has a databank of information on these volunteers—how many had grandparents, parents, or siblings that lived to be 90 or older. "We have the possibility to use this group in a number of ways, as various kinds of control groups," he states.

Wekstein believes that the oldest old in the United States will be studied in much greater detail than in the past, pointing out that persons 85 years of age and over now constitute the most rapidly growing segment of the population.

He cites television programming and advertising as indications of the attention now being paid to older groups. "Look at 'Golden Girls,' for example. The characters are in their 50s, and 60s, and the mother is eighty-something. People over 65 now have the greatest amount of disposable income, so TV ads are being aimed differently—luxury cars and

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vacations and expensive jewelry. There's a whole lot of new public exposure."

Wekstein adds that perhaps the most important finding to emerge from the centenarian study is that in Kentucky, as elsewhere, there is a large number of very old individuals who, as they begin their second century of life, look forward to each new day and add immeasurably to the lives of those around them. ■

Some of the other researchers involved in the centenarian study at the University of Kentucky include Dr. John Thompson, chairman of the Department of Medicine; Dr. Thomas Roszman, professor of microbiology and immunology; Dr. Norbert Tietz, professor of pathology; Dr. Robert Straus, professor of behavioral sciences; and Dr. Anthony DeMaria, professor of medicine.

*Demographic Information about
the University of Kentucky
Centenarian Pool*



	Number of Participants	Percentage of Participants
Sex		
Males	152	30.2%
Females	352	69.8%
Marital Status		
Single	41	8.1%
Married	11	2.2%
Divorced	3	.6%
Widowed	449	89.1%
Living Arrangements		
In own home	61	11.9%
Home of Family	101	19.7%
Long-Term Care Facility	336	65.6%
Other	14	2.8%
Vision		
Excellent or good	99	20.4%
Fair	199	41.0%
Poor	157	32.4%
Blind	30	6.2%

Research on Brain's Self-Repair Mechanism Holds Hope for Alzheimer's Victims

A common belief about the brain is that its circuitry is fixed at birth and that damage to this delicate circuitry is never 100 percent repairable. The idea is, to make an analogy between the brain and a car's electrical system, the wiring is fine when the car leaves the factory, but after years of wear will inevitably short-circuit, or burn out.

At the University of Kentucky, associate professors Stephen Scheff, in the Department of Anatomy and Neurobiology, and Steven DeKosky, in the Department of Neurology, are currently involved in research, funded by the National Institute of Health, that has shown this belief to be false. In experiments with laboratory rats, the researchers have found that the brain directs and regulates a self-repair process after sustaining an injury. There is also some preliminary evidence—and this has important implications in Alzheimer's research—of regenerative or compensatory efforts by the brain in degenerate diseases and in aging.

In their work Scheff and DeKosky cut bundles of connections between specific groups of brain cells in anesthetized rats. Using electron photomicrographs, the researchers are able to count the number of connections between nerve cells, or synapses, in the tissue per unit area and unit volume. As they take more samples, they then plot a time course of regeneration back to the normal levels.

"One surprising finding," DeKosky says, "is that in one area of the brain, before the synapses regenerate to their normal level, they come back at a greater-than-normal level. The older animals have a greater overshoot, whereas younger rats come up just a little bit over normal and then drop down. In other areas there is no overshoot, just a slow return to normal



Steven DeKosky and Stephen Scheff

numbers of connections; although older animals do return to normal, they do so more slowly."

DeKosky states that there are all sorts of "marvelous speculations" why this is so. "In the spinal cord, for example, there are many more cells, motor neurons, than you're going to live with the rest of your life. In development, they send out their axons or signalers to the muscles and those that don't make connections die or are removed. It's a kind of survival of the fittest analogy which also may hold true in the part of the brain we've looked at."

In their work, DeKosky and Scheff have been trying to determine what mechanism controls the regenerative response. So far, they have found a number of hormones that slow or impair the repair process, some of them, DeKosky says, used routinely in head-injury cases. For example, glucocorticoids—a type of steroid—are used to reduce brain swelling in patients after a head injury. These steroids, however, clearly suppress one aspect of the self-repair process of brain tissue. "Now that has serious implications for how we treat patients," he says.

The problem, he explains, is that almost everyone with a head injury needs steroid treatment in order to prevent the brain's swelling inside the rigid brain case. "The idea," he states, "would be to find out why glucocorticoids suppress some reactive growth and to give the patient medication that would decrease swelling with-

out interfering with the re-building process."

A consistent finding in their work relates to the brain's regulation of synapses. "Our work clearly shows that as synapses are lost, the ones that remain get larger, and that might be one of the ways people compensate as they go downhill in their thinking process," DeKosky says. "We've found evidence for a normal relationship between the number of synapses and increase in size as the number drops. An important point is, the brain is doing the regulating and no one thought that happened before."

DeKosky mentions that a number of areas in the brain of Alzheimer's victims have shown a "clear-cut plasticity or regrowth, not unlike the kind of thing we've seen in our experimental models in one of the memory areas of the brain. What happens in degenerative diseases and aging, he says, is that these degenerative processes eventually overcome efforts at regrowth, or that these efforts are weak compared to the pathological process of a disease such as Alzheimer's.

As far as longevity is concerned, DeKosky says that "healthy genetic predisposition" can be taken to mean that a person is a healthy rejuvenator or rearranger of circuitry. "If a man is 85 and in relatively good health," he says, "it may be that wear and tear have occurred just as with everyone else, but that the person has repair mechanisms and reconnection mechanisms that rage strongly against the dying of the light."

Does Dad Have Alzheimer's?

The woman at the other end of the line was obviously upset.

"Dad just hasn't been right lately," she said. "It's hard to say just how he's changed, but he's changed. Could we come in and talk to somebody?"

Since opening its doors in 1984, the Memory Disorders Clinic, located in the University of Kentucky's Medical Plaza, has handled hundreds of requests for information and for clinical help.

"If someone is showing memory changes, personality changes, we like to see that individual and provide a good work-up that would rule out the possibility of any other health problem causing the memory loss," says Ms. Charli Kirkpatrick, Clinical Coordinator. "If we can identify something we can treat, such as a thyroid disorder, that's wonderful—we can fix that—but if not we can do an intense diagnostic study to assure the families we've eliminated the possibility of finding any reversible cause."

Kirkpatrick mentions that a significant number of their patients, approximately 50 percent, come in for second opinions; and some come in for third and fourth opinions. "Local neurologists and internists send us a lot of people. Sometimes they have conducted a thorough evaluation, but feel that the history and pattern of memory loss aren't exact, so they send the patient to us. We also see quite a few patients brought in by families who simply want to exhaust every possibility, to get an opinion from someone who does this exclusively."

The bulk of the Clinic's patients suffer from Alzheimer's Disease, although a few are diagnosed as having Parkinson's disease with dementia and a handful have progressive supranuclear palsy, which is usually accompanied by memory changes.

"We also have some cases that we classify as 'other,'" Kirkpatrick says. "No matter how much we study them diagnostically, we can't identify the specific disease process because the physical changes and memory changes don't fit any classical pattern."



Kirkpatrick characterizes the patient's first visit to the Clinic as "an intensive appointment." During the first hour Kirkpatrick or one of her assistants talks with the patient alone and administers a battery of three "cognitive screening" tests that indicate a level of impairment. While the patient is taking these tests, Ms. Marie Smart, the Clinic's social worker, talks with the family to find out if they have any concerns or needs that she can address.

Next, a doctor gives the patient a cursory general examination, does a detailed neurological exam, and talks with the family, sometimes for as long as one and a half hours, about the specific behavior patterns of the patient and the family's reasons for concern.

If the doctor believes that there is a memory problem, the basic work-up includes blood studies, an EEG and a CAT scan. "We do these tests on an out-patient basis," Kirkpatrick says. "Then we call and generally have the patient and family come back in to discuss the diagnosis. We also send the diagnosis and any recommendations we have to the referring physician if there is one."

"After the patient is diagnosed, the family might be advised to do something as simple as setting up a meals on wheels program for the patient. Or we may advise, in cases of advanced Alzheimer's, that the patient be hospitalized," she says.

Kirkpatrick believes that the Clinic's most important service may be that it provides support across time. "In order to measure changes, it's necessary to take this approach. We like to see the patient every six months. We emphasize that this allows us to learn more about the disease."

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"It's not unusual for a family to call us back a year or so after we do a work-up and say, 'We think Dad's condition has gotten a lot worse.' So we re-test and talk with the patient and the family and can then say, 'Yes, these are the areas we've found to be in decline.'" Generally such corroboration, she says, is a source of relief for the family. Their concerns are validated and they can be told what to look for in the coming months.

Has the Clinic been "successful" in its four years of operation?

"It's difficult to measure 'success' when you're dealing with incurable diseases," Kirkpatrick says. "But I don't think we'd have people calling us and booking appointments and continuing with us if we weren't doing a good job. In 1984 we had about 100 patients. Now we have 430 and that number grows every week."

She adds that in addition to functioning as a support group for families in Central Kentucky, the three physicians and support staff occasionally get "an unexpected surprise."

"A few months ago a woman came in who had been diagnosed as having Alzheimer's. Her family wanted a second opinion. We found that her condition was related to medications, so we changed her medications and now she's fine. She thinks that the doctor who saw her here is a saint. Those are the nicest surprises."



Charli Kirkpatrick

SERVICES OF THE ALZHEIMER'S RESEARCH CENTER SANDERS-BROWN CENTER ON AGING

- * **The Memory Disorders Clinic**—persons with memory problems can be given a complete medical work-up and evaluation
- * **Support groups**—Lexington-area support group on the third Tuesday of each month at 7:15 p.m. in the Sanders-Brown Center
- * **Resource Center on Gerontology**—books, periodicals, films, video-tapes available for loan free of charge
- * **Respite Care**—with the Lexington/Bluegrass Alzheimer's Disease and Related Disorders Association, sponsorship of a day-care program for persons with memory disorders and of in-home volunteers
- * **Free advice and referral**—Center staff will answer questions on Alzheimer's Disease or related disorders and can schedule an appointment to meet in person with staff members
- * **Phone** (606) 233-6040

Alzheimer's: A Personal Account

Shortly after they got married, on September 1, 1947, Betty Morgan remembers her husband Bill supporting her decision to complete her degree in Nursing. Dr. William Morgan told his bride to go ahead and finish, "so if anything happens to me, you can take care of me."

His comment, tossed off jokingly, proved in retrospect to be accurate and ominous.

Betty and Bill were stationed in the New Hebrides, west of the Fiji islands in the Southwest Pacific, in World War II. The two met when Bill's outfit, located two miles from the hospital where Betty worked, showed up one day to build a laundry room for the nurses and to give them a sewing machine and some irons they had commandeered from somewhere.

In early 1947 Bill was working at the Mayo Clinic; Betty was in nearby Wayne University, working on her degree in nursing education. "He stopped by to see me, and we were glad to see each other," Betty recalls. They were married a few months later and settled in Paris, Kentucky, where Bill opened an office.

Betty finished her degree and became Bill's nurse in the office. Their business and their lives flourished for 30 years.

"I remember the day in 1978," Betty says, "when he came to me in the office and asked, 'What's normal blood pressure?'"

"What's the matter?" she asked.

"I don't know. I just can't remember."

These weren't the first signs of a change, Betty recalls. Bill had been irritable and had wanted her nearby. Until recently, he had been affable and outgoing.



At the Lexington Clinic two weeks later, Bill was diagnosed as suffering from diffuse atrophy of the brain. "The doctors said the outer edge of his brain was shrinking, so I believed them. When Bill would ask me what was wrong with him, I'd tell him he was getting to be like his mother, who had exhibited the same symptoms at about his age."

Bill began to gradually decline until there were seemingly only two things on his mind: walking and building fires in the fireplace. He had to be dressed and constantly reminded what to do. And he got worse.

Betty remembers that as a terrible time. "Bill lost his hearing about that time, and people—old friends—shunned us. They 'didn't want to see Doc like this.' He couldn't do anything by himself at that point, and the doctors only thought to drug him with thorazine. I was told to keep him on medicine every six hours."

After two years in Florida, the couple returned to Kentucky. Bill had to have a hernia operation, and doctors finally realized he had Alzheimer's. "I

didn't even know how to pronounce it. This was before there was any effective family counseling, before there were support groups," she says. "And he'd had it for three years."

Betty had Bill re-diagnosed at the Veteran's Administration. It seemed to be a logical place—he was a retired lieutenant colonel and Betty was a retired captain.

"That was one of his worst days. Every response to every question was 'South Carolina.' It's all that was on his mind. For a couple of years I had been writing a book of poems about the disease, and when I gave the social worker a copy, I didn't have to explain anything."

"I got Bill into the Alzheimer's ward at the VA hospital on Leestown Road. The day I took him in, it so happened that an OB nurse that had worked with us in Paris was there. He may not have fully recognized her, but he let her take him off."

Betty visited her husband regularly for fourteen months in the hospital. "The food was so good," she says, "I didn't know what else to bring him. So I brought him a banana each time I came. A few months later when I was walking with him down the hall, he turned to me and said, 'You know, there's this old woman who keeps coming in here and feeding me bananas.'"

On another visit, she remembers him looking around the ward and saying, "It's all so nebulous." "Where," she wondered, "did he find that beautiful word?"

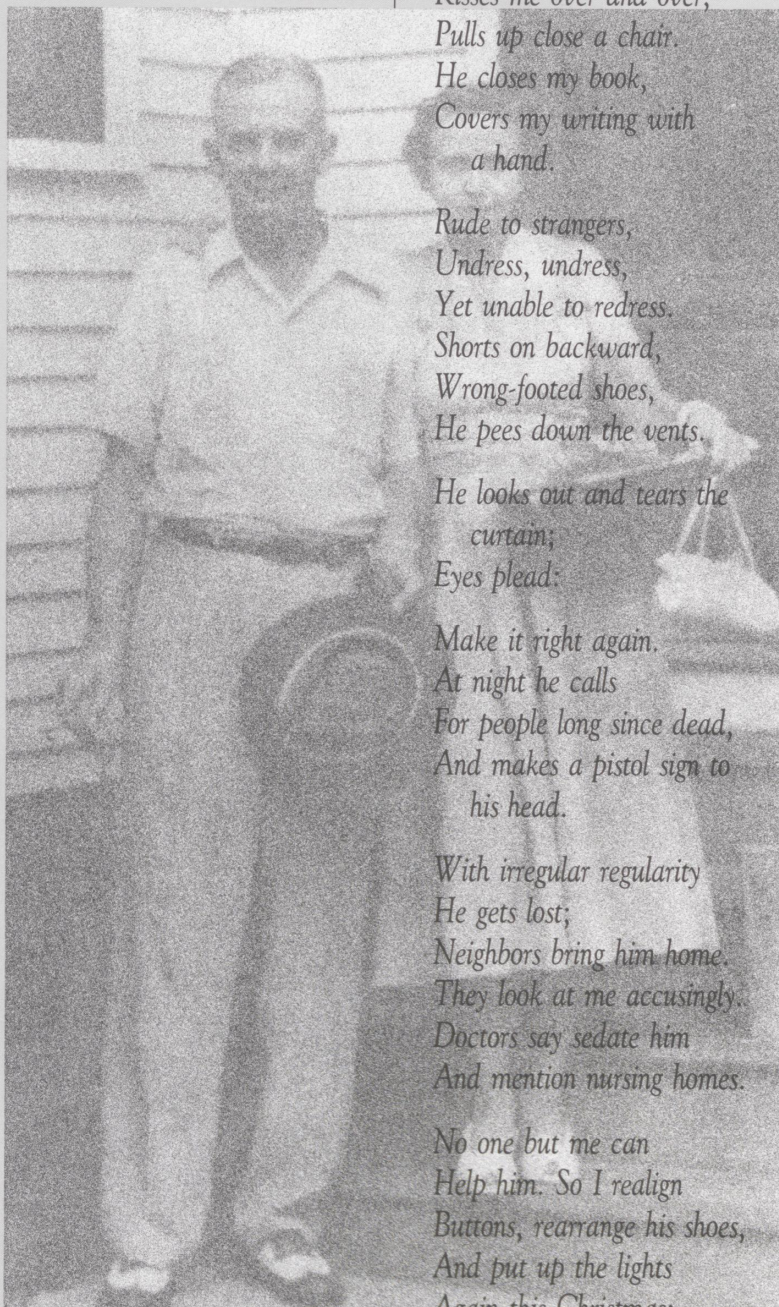
Betty visited the hospital on her birthday, Dec. 31, 1987. Bill was curled up in a fetal position. He had pneumonia. "I got near his good ear and told him it was my birthday—would he sing for me. He sang 'Hap-

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py birthday, happy birthday, dear Billy . . . , singing for me and himself. I never heard him say another thing."

Since that time, Betty Morgan has pieced her life back together. She is a tutor in Operation Read, a docent at the University of Kentucky Art Museum, and is in the Donovan Scholars Program at the University, taking classes on the Lexington Campus. And she continues to write poetry. The following poem is from her book *Alzheimer's Alters Us All*.

Blurred



Bill and Betty Morgan, 1948

He slips into depression,
Clings like a sickly child,
Kisses me over and over,
Pulls up close a chair.
He closes my book,
Covers my writing with
a hand.

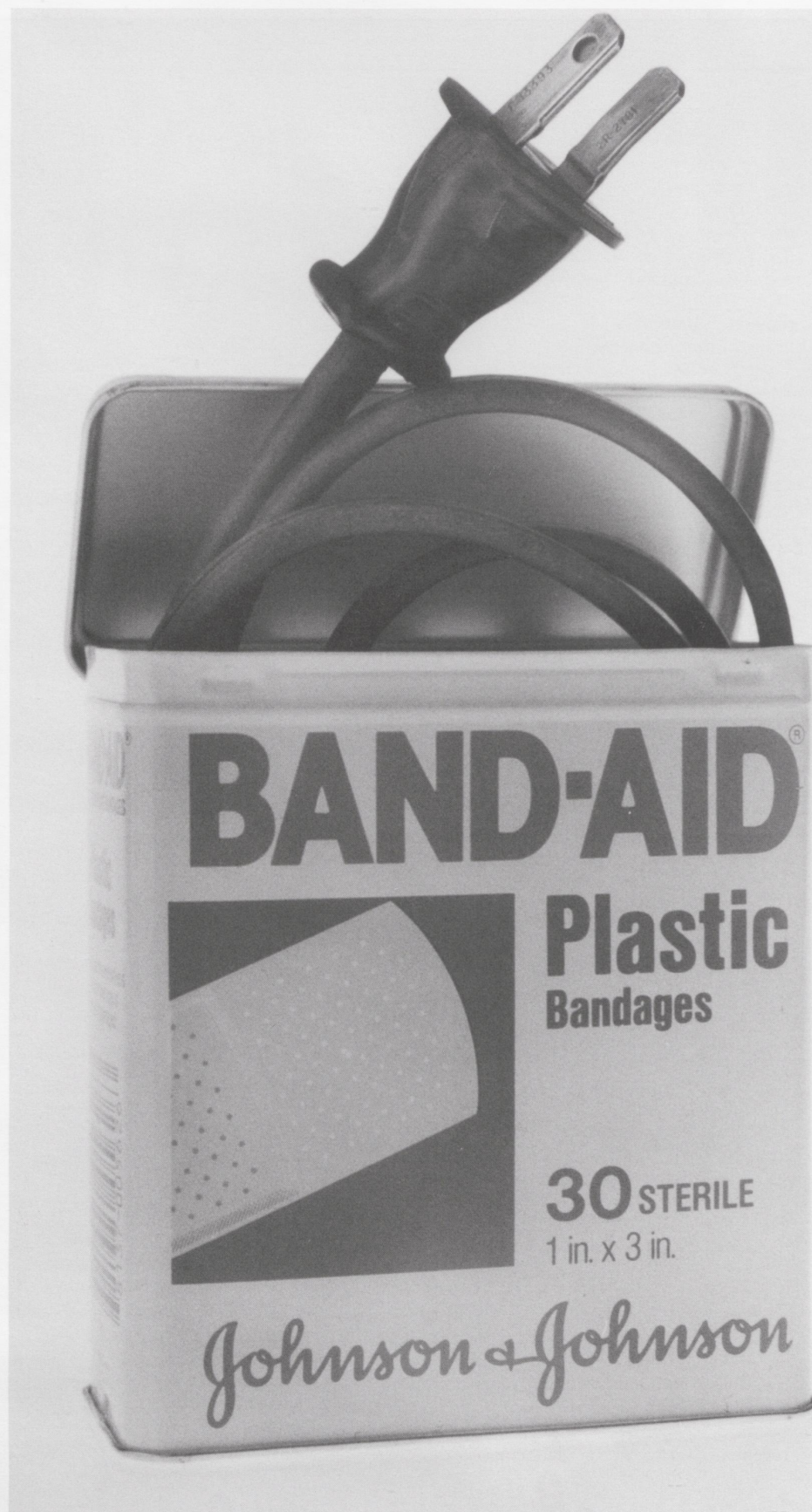
Rude to strangers,
Undress, undress,
Yet unable to redress.
Shorts on backward,
Wrong-footed shoes,
He pees down the vents.

He looks out and tears the
curtain;
Eyes plead:

Make it right again.
At night he calls
For people long since dead,
And makes a pistol sign to
his head.

With irregular regularity
He gets lost;
Neighbors bring him home.
They look at me accusingly.
Doctors say sedate him
And mention nursing homes.

No one but me can
Help him. So I realign
Buttons, rearrange his shoes,
And put up the lights
Again this Christmas;
Though now they blur
with tears.



FASTER HEALING WITH ELECTRICITY:

A Jolt of Black Magic?

by Elizabeth Hansen

An assembly-line worker crushes a nerve in her wrist, temporarily paralyzing her hand.

A teen-ager injured in a car accident needs a skin-grafting operation to repair a wound on his leg.

In the not-too-distant future, exposure to low-level electromagnetic fields might be part of the treatment for both of these people.

When a nerve is crushed or severed, muscles in the part of the body affected begin to waste away, or atrophy. The more quickly the nerve regenerates or repairs itself, the less damage occurs to the muscle. Lack of blood circulation hinders healing of wounds and is one reason surgical transplants such as skin grafts die.

Exposing the damaged nerve or tissue to low levels of electrical stimulation appears to speed regeneration of nerve tissue and improve circulation by increasing growth of new blood vessels. That's what Dr. Betty Siskin and colleagues have found in studies using rats.

Electricity has been used to speed healing of bone and cartilage injuries for over 10 years, according to Siskin, research associate professor in the Center for Biomedical Engineering at the Wenner-Gren Research Laboratory and adjunct research associate professor in the Department of Anatomy and Neurobiology of the UK Medical School. She has been studying the regenerative effect of electromagnetic fields on nerves since completing her Ph.D. at the University of Kentucky in 1973. Physi-

cians may be applying her findings to humans within a few years. Already doctors elsewhere are using electricity in certain skin-grafting procedures and to treat ulcers.

Most of Siskin's early work on electric field effects was done in a laboratory dish using cultured nerve tissue from chick embryos. A few years ago she began working on nerves that were cut. Then in the spring and summer of 1987, with funding by the American Scandinavian Foundation and The Swedish Institute, she spent three months at the University of Lund in Sweden. There she worked on crushed sciatic nerves in the legs of rats.

A crushed nerve, Siskin says, "is a very frequent type of injury as opposed to a nerve that is completely severed." The majority of nerve injuries to people involve crushes rather than complete cuts.

In the Swedish study, rats were anesthetized and an incision was made in a leg. The sciatic nerve was crushed using special pliers and the incision was closed. Then for four hours a day for six days the rats were placed between two Helmholtz coils, large wire circles placed about eight inches apart, through which the electromagnetic field was transmitted. The results surprised even Siskin and her colleagues.

"It all looks like black magic. The first experiment we did was positive, and it's just never failed. I still don't believe it," she says.

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While a crushed nerve will eventually recover almost completely even if not exposed to electromagnetic fields, faster healing has benefits. "When you speed up this recovery, what you are doing is minimizing the amount of atrophy of the muscle. The longer the nerve is not restored, the greater the chance that muscle will undergo some atrophy," she says.

Before Sisken's findings can be applied to people, several questions must be answered. Sisken plans to investigate how and where to apply stimulation to get the maximum effect. "It's one thing to have animals between two Helmholtz coils and treat the whole animal. We certainly wouldn't do that to humans," she says. "Suppose you crush the nerve going to your hand muscles. Does the physician have to put all of you in a coil? Could some coils be put just over the injury or can some coils be used to stimulate only at the source of the nerve, which is really in the spinal cord?"

While Sisken is studying regeneration of crushed nerves, other researchers are examining the effects of electromagnetic fields on severed sciatic nerves in rats. Dr. Michael Orgel, a plastic surgeon at the Berkshire Medical Clinic in Pittsfield, Massachusetts, compared rats in which cut nerves were sewn back together immediately to rats in which the repair was delayed five days. Both groups were treated with the same low-level electromagnetic fields while a control group was not exposed to the fields. What Orgel found, according to Sisken, was that animals in which nerves were repaired and treated immediately did not do much better than the untreated control group. However, animals in which repair and treatment were delayed did better than the control group and those treated immediately.

In presenting their findings to the Society for Neuroscience in November [1988], Sisken, Orgel and other researchers concluded that their results "demonstrate that pulsed magnetic field treatment with the appropriate clinical regimen could become a treatment modality for various nerve injuries."

Sisken's research on the effects of electric and electromagnetic fields on wound healing

“ It all looks like black magic. The first experiment we did was positive, and it's just never failed. I still don't believe it. ”

has been funded by Bioelectron, a company which makes equipment used to produce these fields, and the Office of Naval Research. Although the projects involved applying the fields in different ways to laboratory rats, in both cases blood circulation was increased in treated animals compared to those that were not exposed to the fields.

In the already-completed Bioelectron study, four Ivalon sponges were implanted in incisions on the backs of rats. Electrodes were attached to each animal. Some of the rats received no exposure to electrical stimulation, some were exposed 24 hours a day, and some were exposed for 12 hours a day, followed by 12 hours without stimulation. The sponges, each only about a fourth the size of a dime, were removed after one, two, or three weeks. Analysis showed increased blood vessel growth in sponges taken from animals which had been exposed to electrical stimulation, with more growth occurring in animals in the 12-hours-on, 12-hours-off group compared to those stimulated continuously.

"The final bottom line is that the circulation to the sponge was increased by the electric fields," Sisken says. "By having an increased circulation, you have a greater chance for the wound to heal."

Funded by the Office of Naval Research, the three-year project, which runs through June 1989, has also found increased blood-vessel growth due to exposure to electromagnetic fields. In this research Sisken is collaborating with Dr. Ewa Herbst, an electrical engineer in the Department of Biomedical Engineering at



Betty Siken

Tulane University in New Orleans. Herbst was formerly with UK's Center for Biomedical Engineering.

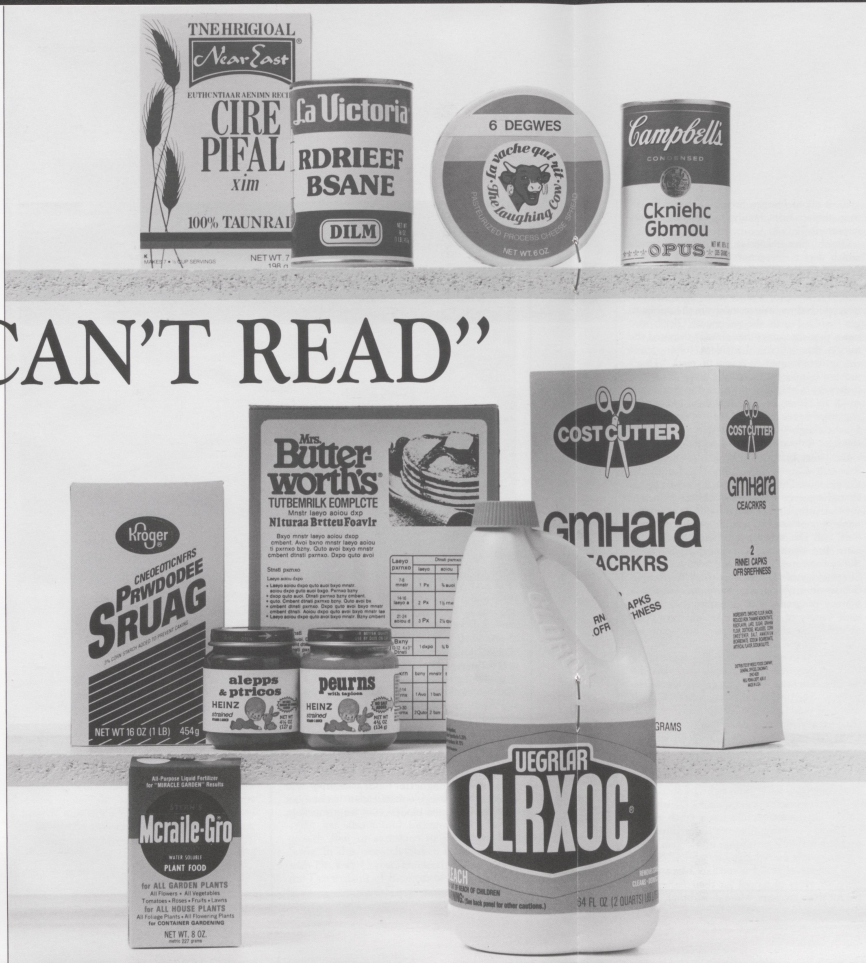
In this study, rectangular skin flaps made on the backs of rats were exposed to low-level electromagnetic fields. After seven days, the flaps were examined using computerized image-enhancement techniques. A portion of the flaps died. "We all think it is due to lack of circulation," Siken says. In animals treated with electromagnetic fields, healing was speeded up. Image-enhancement techniques revealed increased blood vessel length in flaps

taken from the treated animals.

Siken's and Herbst's findings, if supported by more extensive studies, should have immediate applications in surgical transplants for people. Lack of circulation is one of the main reasons surgical transplants die.

Siken wants to focus her future research on nerve regeneration studies, but funding could be a problem. Her work using crushed nerves is currently unfunded. "There are very few sources of funding to look at how electromagnetic fields can be used for regenerative process," she says. "It is difficult always to find money for research on bioelectric effects." ■

"I CAN'T READ"



Kentucky Literacy Program Hopes to Change a Debilitating Reality

by Gary Pierce

Mary Frazier's voice is slightly unsteady as she reads the words, but her will is strong enough to get her through the ones she has difficulty pronouncing. "To me, education means I will be able to do what I was cheated out of as a young person," she reads. "I will be able to get a job with better pay than I have now. When I get my diploma, I will be able to help other people who can't read. "But best"—she momentarily loses her place, then recovers—"without education I wouldn't be able to help them. Education means a whole new life for me. I am very excited about it. I want to see what is waiting out there just for me to find and do."

She pauses, then adds with no little pride, "That's something I wrote."

Such an accomplishment seemed an almost impossible dream for Frazier, age 54, when she enrolled in Henry County's adult literacy program just over a year ago. Now, she says, "I'm just about ready to take my pre-GED."

With a grant from the Ford Foundation and the help of the University of Kentucky Survey Research Center, UK's Center for Developmental Change is working with the Kentucky Literacy Commission to conduct a longitudinal study of students like Mary Frazier who are enrolled in the many statewide literacy programs funded under the Commission's auspices. These programs operate at the grassroots level, with one paid coordinator working to match a fluctuating corps of volunteer tutors with adults who want to learn to read.

The Ford Foundation is particularly interested in studies to improve opportunities in rural areas, according to Cynthia Duncan, who oversaw the Commission's grant proposal for the Foundation. "The literacy program fits into that rubric," she says, "because the first component of any developmental movement is having skilled workers and building the base of human resources. Ford is interested in wedding community development organizations and people at the grass-roots level with researchers, scholars and leaders at a level where they have a responsibility for more people and more money."

With the first wave of data tabulated from the January and February 1988 survey and the second wave still to come in early 1989, many

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questions remain unanswered. Mary Frazier, however, doesn't have to think twice about what prompted her to learn to read. "I'd hear about jobs, and after a while I got to where I'd ask before I'd go see about it," she recalls. "I'd say, 'Well, do they have to have their high school?' and they'd say 'Yeah,' and it'd be almost twice what I was making. And it'd almost make you sick, knowing it was there and you couldn't get it 'cause you didn't have your education."

According to the 1980 Census, Kentucky leads the nation in an ugly statistic—having the highest proportion of adults who failed to complete at least eight years of formal education. That makes the Commission's study all the more vital. "It's the first attempt on a statewide level to monitor progress for a long period of time," says Patricia Gleich, the Commission's executive director. She adds that the study has already begun to dismantle some of the stereotypes of illiteracy. "The assumption often is that these people are dumb. They're not dumb. They've had to develop some fairly sophisticated coping mechanisms to get through life without being able to read. We're finding that the biggest block is lack of infor-

mation about literacy programs. Second, getting support from family and friends is very important."

Gleich cites television ads about literacy which depict emergency situations such as a misread medicine bottle. The implicit message, she argues, is that illiterate persons are like bombs looking for a place to explode, a depiction which does little to motivate the public to get involved with the programs. Gleich also notes that the survey has already disputed the notion that a "critical incident" often drives the undereducated to learn to read. "That's just not usually the case," she says. "It's not as if they say 'Omigod, I must learn to read today or I'll die.' It's more a gradual thing of realizing the importance and satisfaction of reading. Maybe they've always figured the steps were there for someone else but not for them."

Dr. James Houglan, director of the Survey Research Center and acting director of the Center for Developmental Change, agrees that the survey points out the importance of the intrinsic desire to learn, but adds that awareness of existing reading programs in the area and the support of friends and family were also significant factors in the students' decision to enroll. Houglan, also a professor of sociology at UK, stresses that "it's dangerous to do any stereotyping about persons in literacy programs. For example, they hold a wide variety of jobs. Some are not very desirable because of the low pay, but some are higher-paying jobs."

The survey has found that 48 percent of the students are working full-time, with the disturbing downside that 44 percent are unemployed. The average income level of those surveyed is \$11,863. The statistically "typical" student is 37.6 years old, male (63 percent), white (79 percent, although in Louisville, 86 percent are black), and has spent 8.6 years in formal education. Eighty-four percent have less than a high school education, and 40 percent completed fewer than eight grades.

"Illiteracy is inter-generational," Gleich says. "If I'm illiterate, my child has a much greater probability of being illiterate than yours. The problem is that a percentage of problem learners are simply passed along in school." Survey respondents reported a median education of only 5.9 years of school for their fathers and 8.4 for their mothers. More disturbingly, while

“ People who can't read aren't dumb. They've had to develop some fairly sophisticated coping mechanisms to get through life without being able to read. ”

parents most often dropped out for financial reasons or to go to work, their children quit for sheer dislike of school, disciplinary reasons, pregnancy or marriage. For the adult students, the problem was often beyond their control. For their children, the problem seems to stem from poor personal motivation.

Although many students, like Mary Frazier, reported better job opportunity as a reason for enrolling, the intrinsic desire to read and write was most often cited. Elaine Johnson, coordinator for Henry County's adult literacy program, says of her students, "Most want to learn to read just to be able to. . . . Some have put kids through high school and they're so proud, and now they want to do it, too. . . . Most of them feel bad about themselves when they first come in, but once they start they're not ashamed anymore. It's great to finally see them open that door and come in smiling."

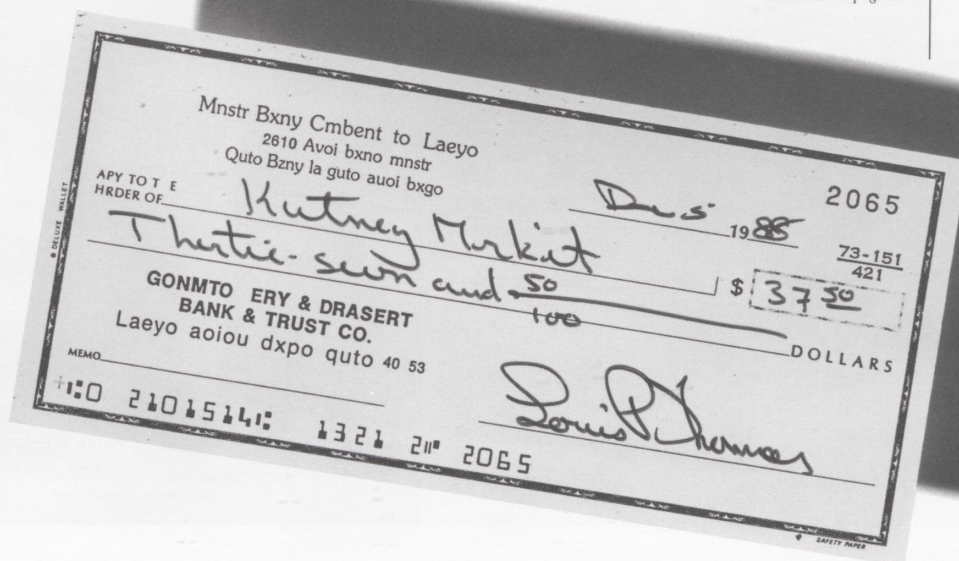
Even armed with the determination to learn to read and write, students face another, perhaps more imposing, barrier: their own fear of embarrassment. Ronald Horseman, a 44-year-old student who has been in the Henry County program for a year and a half, knows all about that fear. "Keeping my secret hid," he says, "that's the toughest thing I had to do. The hardest part is taking that first step." (See sidebar "One Man's Story.")

The easy equation of illiteracy and stupidity is another barrier many illiterate adults face. "Somehow we have to get through that stigma that if you're illiterate, you're stupid," says Ann Lieberman, Trimble County's coordinator. "We need a better referral system to pass on the names of people who can't read. Grocery store clerks know who they are. They're the ones who fill out their checks for them."

Oldham County coordinator Beth Parrish agrees. Fear of being discovered illiterate keeps them from "having a clerk lead them through the aisles to find items. They have to eat the same things all the time because they don't want anyone to know." Parrish also says money alone won't solve the problem. "The students we get are ones who have failed in the school system, so I'm not convinced that more money is such a good solution. There are always problems the school system can't meet, and literacy programs are filling that gap."

Nonetheless, finances are still a source of difficulty for literacy programs. The Commission's report on the survey findings recommends initial screening of participants along the scales of value orientation toward education and purposefulness, which have proven to be useful predictors of student satisfaction with literacy programs. Clearly, however, screening individual literacy programs and

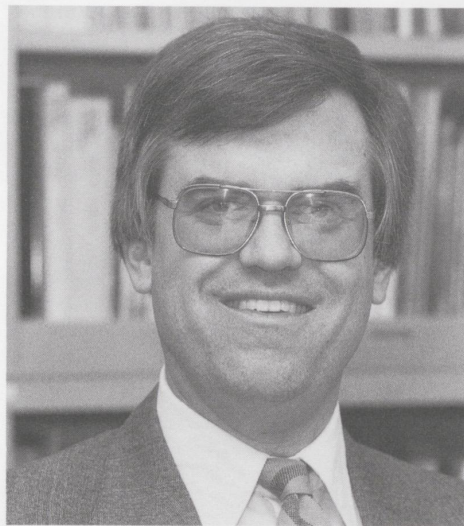
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Many students choose to go public with their stories, Horseman says, once they see the benefits of literacy programs and the support behind them. Horseman now devotes a great deal of his time to helping out with the Henry County literacy program. "I'll talk to anybody about it," he says of his remarkable journey into literacy. "I'd tell the world about it. It's just something that I'm a 100 percent believer in. My wife keeps asking me if I want to move my bed to the library or just put it somewhere in between."



James Houglan

active students. "We've only had two tutors quit in a year and a half," Redmon says, "and we always have a list of people who want to be tutors. What with all the new manufacturing and the Japanese moving in, we're offering English as a second language . . . It's hard work and you have to get out and do a lot of PR, but it's really worth it when they send you flowers or write you a letter."

Unfortunately, it isn't all letters and roses for literacy programs. Ohio County coordinator Layce Kassinger says her program can't afford a computer. "Are you kidding?" she says, "We're lucky to get a corner in the Board of Education. We're talking shoestring budget here." Kassinger also cites the size of her county and its widely scattered population as serious drawbacks, creating transportation problems for both tutors and students. Such physical obstacles do nothing to alleviate the motivational problems that often set in as lessons become more difficult and the day-to-day rewards less dramatic for the students. "So many of them lack stick-to-it-ness," she laments.

Money is certainly not the motivation for those aiding the illiterate, since the coordinators are the only ones paid and at that only barely. Lieberman says she gets about \$110 every two weeks. Moreover, after a 12-hour initial training course, volunteer tutors spend

from "45-50 hours with the average student in order to increase about one grade level," she says. "And that still does not mean that they'll have all the word recognition skills of those who've finished first grade."

Still, the rewards are immense, Lieberman says. "It can be heartbreaking if you're not properly prepared," she says of the teaching process. "You have to break down the process into day-by-day steps. Maybe they want to read the Bible or get their driver's license. So you say, 'OK, driver's license in six months, possibly.' So maybe they learn five road signs each week, just see some progress each week. It can be extremely frustrating, but when these little goals are met, it can be exciting. I had a student tell me the other day, 'I read all the signs on the way to Louisville. First time in my life.'"

“I read all the signs on the way to Louisville. First time in my life.”

Such triumphs are out of reach for many of Kentucky's undereducated adults as long as literacy programs labor in relative obscurity, battling prospective students' fears of being discovered illiterate. "The toughest part is admitting they have a problem," she says. "I'm glad to see more awareness from the publicity about the adult undereducated. The funds have been cut back but you hear more about it now. As long as it's kept secret, no one is likely to step forward."

Mary Frazier is happy she's taken that step. She hopes to take her GED test soon and then find a better job than at the Crossroads Truck Stop where she is currently employed. In the meantime, she has more immediate rewards to keep her going. "I got a notebook," she says, "the kind that's got the line down the middle of it. I had it filled up on both sides with words I didn't know. I went back and read it the other day, and I had just about only one side of words I didn't know. I'd learned all that extra. I was excited about all the new words I did know." ■

SLEUTHING THROUGH THE STABLES

by Linette L. Wheeler

The horse in the box stall appeared calm and content. It shifted its position and moved about, averaging about two steps per minute with the left foreleg. Then two minutes later, following an injection of a narcotic drug, that same horse was trotting around the stall at more than 25 times the norm, or about 80 steps per minute. Put that horse on a race track, and she'd probably be a winner.

Of course that would be illegal, but that hasn't stopped some dishonest horsemen from using such stimulant drugs to improve a horse's performance on the track. They've been doing it since the late 1800s and, unfortunately, some are still doing it today.

For years, racing authorities have been playing the game of "catch up with drugs." Each time a test is developed to detect a drug, someone discovers a new one to take its place. Standard post-race tests can't always identify the presence of a narcotic or stimulant, and even if they could, the amount injected is often too small to be detected.

Enter the ELISA (enzyme-linked immunosorbent assay) for equine drug testing, recently developed and adapted for use in racing under

the guidance of Dr. Thomas Tobin, director of the Equine Drug Research Program in the Gluck Equine Research Center at the University of Kentucky.

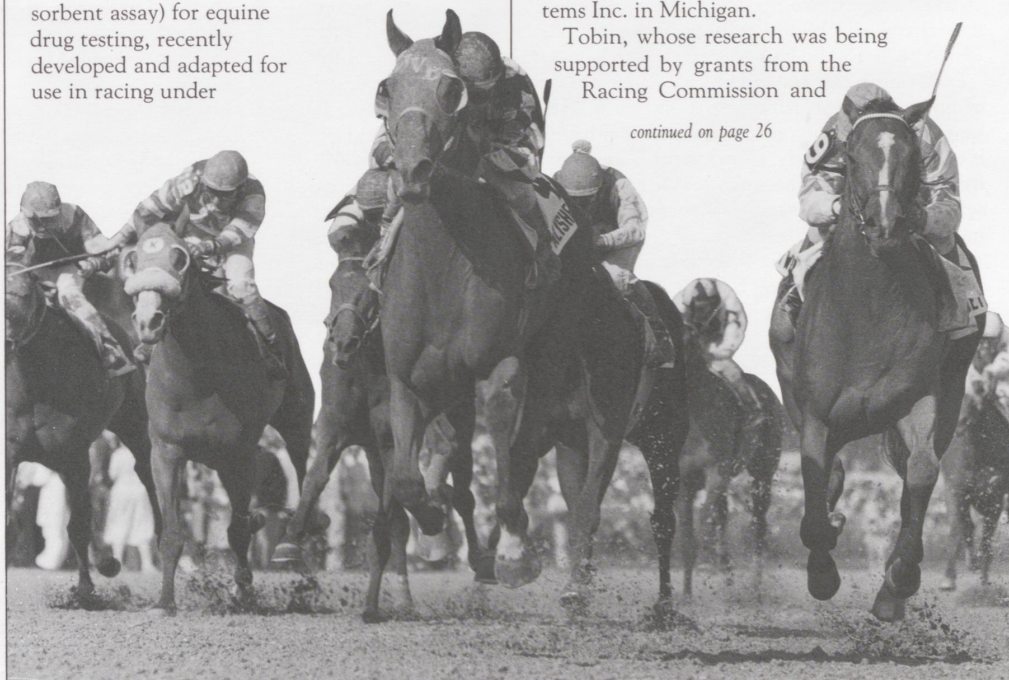
"ELISA tests are not new," says Tobin. "They have been around for several years and are widely used in infectious disease work. The test used to screen for AIDS is an ELISA test. We're using the same method but have adapted it for drug testing."

Tobin was offered a position at the University of Kentucky in 1974 to set up a research laboratory for studying the detection, actions, effects and uses of medications in race horses. Today, the results of that research are causing a major upheaval in the horse racing industry.

In 1986, two events focused attention on Tobin's research. The Kentucky State Racing Commission and the Equine Drug Council initiated a research program to develop new tests for high-potency drugs that were being abused in horse racing. At the same time, the Illinois Racing Board began to develop a pre-race testing program and requested technical assistance from International Diagnostic Systems Inc. in Michigan.

Tobin, whose research was being supported by grants from the Racing Commission and

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the Drug Council, had worked closely with these groups. They hoped Tobin's ELISA would be the stringent program that was needed.

Tobin emphasizes the importance of collaboration in the program's development. "I'd like to think that I had a lot to do with it, but it wouldn't have happened without the cooperation and contributions of others, including UK's College of Pharmacy and the Department of Chemistry."

The result of this collaboration is a panel of equine drug tests that are up to 500 times more effective than other standard, drug-screening procedures. By October 1988, about a dozen ELISA tests were available for use on specific drug families and as many more were under development.

The first step in creating an ELISA for a drug is the most time consuming. An antibody, a chemical derivative of each drug, must be synthesized and then developed for each drug family in laboratory rabbits, a process that takes about three to six months. A good antibody fits the drug like a lock fits a key, and this coupling is the basis of the sensitivity of these tests. Once the antibody is obtained, it is chemically bound to a clear plastic well, which becomes the basic test unit.

Performing the test involves adding a drop of horse serum or urine to the test well. If the sample contains no drug, there is nothing to bind to the antibody and the antibody is left free. After an enzyme wash and a color development step, the sample turns blue, which indicates a negative test.

A positive test results when a drug is present in the sample. The drug binds to the antibody and in the final development the sample well remains clear. These positive tests signal a "hit" that is then investigated further.

The advantages of using the ELISA is that it is simple to do, the results are immediately visible, and it is sensitive not only to major drugs but to closely related agents. It's also quick; a test can be run in about 30 minutes.

The speed and efficiency of the ELISA were determining factors when the state of Illinois decided to use pre-race testing at certain tracks in 1987. Most states test horses after they have run, and a horse can be disqualified and trainers suspended for using drugs.



Graduate Assistant
Thomas Wood and
Thomas Tobin

According to a New Mexico Racing Commission investigator, there have been 66 positive tests in that state during the last year, involving a total of about 47 people. Of those, more than a dozen trainers have been suspended and investigations are continuing.

Horses can be injected with narcotics or stimulants, or with both. The running effect produced by opiate drugs can be intensified and prolonged when opiates are used in combination with stimulants. Because many of these drugs are so potent, it may take only 50- or 100-millionths of a gram to produce the desired effect. Such minute amounts, in many cases, were impossible to detect before the development of the ELISA test.

Until recently, the basic detection method for drugs has been thin-layer chromatography. In this method, a urine sample is placed onto a glass plate, covered with a thin layer of silica gel, and then developed in a solvent which separates the urine from any drug present. The dried plate is sprayed to develop colors in the different compounds; certain colors will represent natural urine components and some will represent drugs. Unfortunately, many drugs escaped notice with this method.

Tom Wood, a Ph.D. candidate who has worked with Tobin for the past four years, thinks the ELISA tests are "changing the way we test for drugs."

"The ELISA can be adapted to any kind of chemical molecule, as long as you can raise the antibody for it. The thing to remember is that this is a screening test. When there's a strong suspicion of drugs present in a [blood or urine] sample, then there's a need for further testing and confirmation."

A strong suspicion of drug abuse was exactly what turned up in New Mexico when the ELISA test was used there. On Labor Day, 1987, Elans Special won the \$2.5 million All-American Futurity for Quarter Horses. According to a January 1988 report in *The Albuquerque Journal*, the two-year-old filly ran with a bruised foot and still won by 1 3/4 lengths. Initial post-race tests gave no indication that drugs had been used to boost her performance, but follow-up tests using the ELISA method showed Elans Special had run under the influence of oxymorphone, a relative of morphine.

Wayne Conwell, an investigator with the New Mexico Racing Commission, says there have been 66 positive tests in that state during the last year, involving a total of about 47 people. Of those, more than a dozen trainers have

been suspended and investigations are continuing.

Conwell's opinion of the ELISA test is simple and to the point—"It's good."

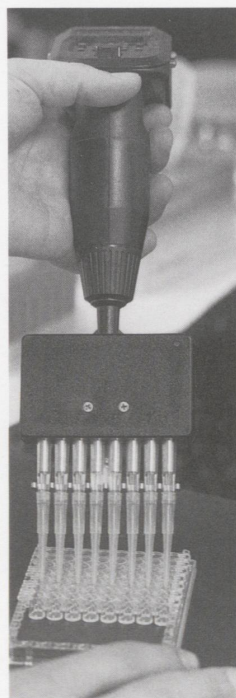
In Oklahoma, ELISA tests were good enough to shake up the trainer standings in that state. Tobin assisted the Oklahoma drug-testing laboratory by screening some of its equine urine samples for Sufentanil. This potent narcotic was not being detected by standard tests, but Tobin and his associates uncovered about ten positives out of 200 samples. Because of their findings, the second place trainer moved up to first place in the Oklahoma standings.

In Kentucky ELISA tests are used, along with other procedures, in the hope of eventually establishing a drug-free horse environment. Every day during racing season, a new

batch of test samples is delivered for screening to the lab of Dr. Jerry Blake in the Gluck Equine Center.

Lyle G. Robey, chairman of the Kentucky State Racing Commission, says, "Success is measured by how many negative tests we get. When some tests were first done for one of the more exotic drugs at Turfeland in 1987, about five positive tests turned up very quickly. Since then, there's been no more. Word gets around and it [the use of those drugs] stops."

The use of illegal drugs on the nation's horse racing tracks may continue, but Tobin's research and the implementation of ELISA in several states has put dishonest horsemen on notice. Kentucky, Illinois, New Mexico, and Oklahoma have already shown that ELISA is a test that gets results. ■



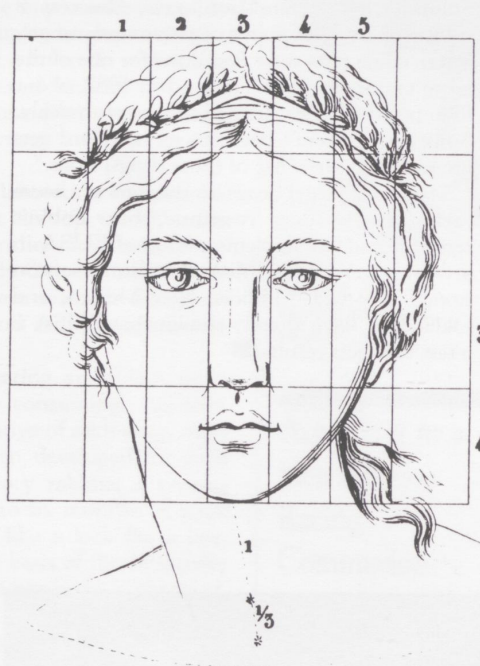
A multi-channel pipette is used in the batch testing of horse urines. Newly developed ELISA tests are more efficient than previous tests in detecting the presence of illegal drugs.



STEROIDS AND SEXUALITY:

Studying Effects on the Female Central Nervous System

by Michal Smith



Uncharted territory holds a special fascination for Dr. Robert Watson, an assistant professor in the Anatomy and Neurobiology Department of the University of Kentucky School of Medicine. Every summer, the power of that fascination lures Watson and his wife, Sonia Carlson, a post-doctoral fellow in the Department of Microbiology and Immunology, canoe in tow, into the remote wilds of the "north country."

With only a topographical map and a compass for guidance, the couple spent two weeks last summer canoeing through pristine, virtually uninhabited parts of the Arctic watershed in northern Ontario. "Sometimes," says Watson, "we went five or six days without seeing another human being."

The topographical maps of wilderness areas on the walls of Watson's office mirror enlarged photographs of a region of the brain that has captured his scientific imagination. The maps

and photographs have a similar attraction for Watson: both invite the explorer to chart the unknown. This desire has led him to the last real research frontier in anatomy—the vastly complex central nervous system.

"I really viewed the central nervous system as the one area about which so much was not known, an area that controls so much," Watson recalls.

A boyish-looking 35, Watson was appointed to the Anatomy and Neurobiology Department in May 1987 after completing five years of post-doctoral training at the University of Rochester School of Medicine and Dentistry. Principally a researcher, Watson now teaches two courses—a primary anatomy course for medical and physical therapy students and a graduate course in cell biology for Ph.D. candidates.

Though the demands of teaching encroach upon Watson's time in the laboratory, he finds pleasure in the spark of connection that teaching offers. "I enjoy it for the immediate feedback you get," Watson says. And his students seem to enjoy this interaction as much as Watson does. It is not unusual to find a number of them crowded in Watson's already-cramped office, seeking elaboration on a lecture or specifics about an upcoming examination.

Watson completed his undergraduate work at Colgate University and then spent a year working as a technician in a neurosurgery lab at Albany (New York) Medical School. He then went on to pursue a Ph.D. in physiology at the University of Medicine and Dentistry of New Jersey. Throughout his training, beginning with his pre-doctoral studies of aggression and mapping of neuronal pathways activated during an epileptic seizure, Watson has been fascinated by neurotransmission, what he terms the 'wiring' of the central nervous system.

These cell-to-cell interactions, triggered by the chemical substances secreted by neurons, are the focus of Watson's ongoing research on the hypothalamus and preoptic regions of the

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brains of laboratory rats. In these areas there are distinct anatomical differences between the male and female. These same regions of the brain are also "sexually dimorphic" in humans; as with the rat brain, they are located in an area known to regulate sexually differentiated processes, such as endocrine function and ovulation through actions exerted on the body's "master gland," the pituitary. This area also regulates reproductive, maternal, and aggressive behavior.

Now three years along a research path that began at Rochester, Watson has discovered that this region of the female rat brain is "strikingly different" from that of the male. Specifically, Watson has identified a collection of nerve fibers that express an opiate-like neurotransmitter (Met-enkephalin) in only the female brain. No such communication pathway is evident in the male brain.

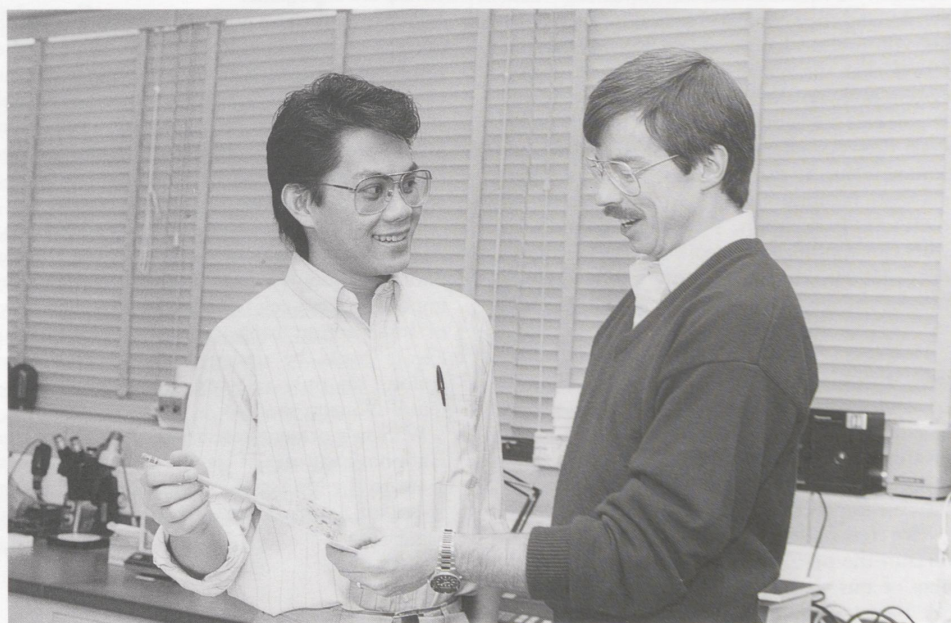
Employing a process known as immunocytochemistry, Watson has documented various steroid-induced neurochemical changes in the brains of female rats. Working with Graduate Assistant Chris Langub, Watson deeply anesthetizes the animals with sodium pentobarbi-

tal and injects a formaldehyde-based solution. The brain is removed and sectioned on a microtome, an instrument for cutting thin slices of tissue. These slices are immersed in solutions of antibodies to Met-enkephalin, which, in effect, "stain" the fibers to which they are drawn, illuminating the distribution of these neurotransmitter substances in the brain. The extremely delicate tissue is gingerly transported to the solutions with an artist's paintbrush. Finally mounted on glass for examination, the brain sections are so small that four of them would fit on a postage stamp.

Using this procedure, Watson found that if the ovaries, the source of estrogen, are removed, the uniquely female neurochemical system simply disappears. The female rat's brain becomes indistinguishable from the male's. Replacement of estrogen after ovariectomy results in the female-typical neurotransmitter system again being expressed. In older subjects, Watson has discovered that the brains of post-menopausal female rats also

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Graduate Assistant Chris Langub Jr. and Robert Watson



STEROIDS AND SEXUALITY

appear to be like those of the male. In his current experiments, he hopes to discover if the re-introduction of estrogen will revive the typically female neurochemical system.

Earlier experiments revealed that when prepubertal female rats were exposed to elevated levels of estrogen, the distinct female neurochemical system ordinarily detected only in the brains of mature females appeared. The presence of steroids accelerated the presence of the met-enkephalin system in the brain.

Working with his former mentor, Dr. Gloria Hoffman, a nationally known researcher at The University of Pittsburgh, Watson also hopes his present research will ultimately provide a greater understanding of the role that steroids play in the development of the central nervous system.

It has long been assumed that sexual differentiation of the human brain occurs before birth. With rats, however, some elements of sexual differentiation occur after birth. But that process, Watson has found, can be permanently altered when the steroidal environment is manipulated.

When newborn female laboratory rats were exposed to the male hormone testosterone, they experienced physical and behavioral changes. Ovulation ceased, rendering them sterile, and they exhibited sexual behavior typical of males. Upon examination, Watson found that the female-typical met-enkephalin system had vanished. The brains of genetically female rats appeared no different from those of male rats. An alteration of the steroidal environment during development had caused permanent, life-long changes in the circuitry of the brain. In addition, Watson has found that with the appropriate steroid treatment during development, the male brain can be permanently changed to express the female-typical neurotransmitter system.

However, Watson cautions that a clear cause-effect relationship between the altered neurochemistry of the brain and changes in physiology and behavior has not yet been established, though the possibility clearly exists. This relationship will be the subject of future experiments.

"We have identified neurotransmitter systems in the brain that can be altered by products of our endocrine system. These steroid

Behavioral characteristics such as aggression and even sexual preference could be influenced by steroid exposure during the development of the central nervous system.

hormones provide feedback to the central nervous system and can profoundly alter brain neurochemistry," Watson says.

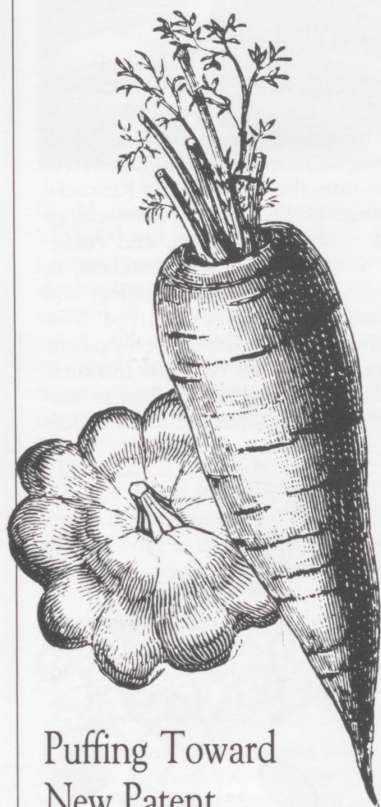
Watson's experiments indicate that exposure to an altered steroid environment during development produces permanent effects in the sexual differentiation of the brain. Such exposure could be the result of inherent problems with steroid metabolism. Alternately, steroid exposure during development could result from contact with naturally occurring estrogens which are synthesized by certain plants and, as a result, may enter the food chain. He also mentions that by-products of certain pesticides are estrogenic.

Problems such as infertility, which affects 15 percent of U.S. couples, may be, in part, the result of central nervous system problems caused by steroid exposure. And behavioral characteristics such as aggression and even sexual preference could be influenced by steroid exposure during the development of the central nervous system.

"If we can learn everything we need to know about how these neurons are talking to one another, about what types of signals are important from cell to cell, then the possibility of intervention exists. New pharmacological agents could be designed with very precise actions on only selected neurochemical systems," Watson says.

Watson's present research is funded by the National Institutes of Health through a parent grant to the University of Pittsburgh, and by a series of internal research and equipment grants. ■

RESEARCH BRIEFS



Puffing Toward New Patent

Plumped-up carrots? Puffed-up peppers? Dr. Fred Payne, University of Kentucky agricultural engineer, has developed a process that "puffs" dried vegetables before they are reconstituted. The result, Payne says, is a product that re-hydrates more quickly than freeze-dried vegetables and is more pleasing to the eye than air-dried vegetables. An application to patent the process is "in the works."

Payne explains that the conventional method of puffing cereals, such as puffed rice and puffed wheat, involves cooking the products with steam first and then releasing it quickly. The sudden release of the steam expands the cereal much like kernels of popcorn popping.

Payne's method does not require heating the food first. It uses carbon dioxide which penetrates the vegetables. When the carbon dioxide leaves the vegetables, they puff. The advantage to Payne's process is that the vegetables become more porous, allowing them to take up water more quickly than dried vegetables do.

"Freeze-dried vegetables also take up moisture quickly for reconstituting, but the process for freeze-drying is very expensive—several times more expensive than drying them," Payne says. His process is slightly more expensive than drying, but he believes industry may find the added cost insignificant compared to the advantages of the puffed vegetables. His device can puff a pound of vegetables for about four cents worth of carbon dioxide.

Payne says there is a good possibility of industrial support with his process-related research, beginning in early 1989. "One of the things we want to investigate soon is to see whether the puffing process changes the nutritional and taste qualities of the vegetables," Payne says.

—Randy Weckman



Dissertation-Year Fellowships

In order to enhance the research dimension of graduate education at the University of Kentucky, President David Roselle has provided funding to support ten to 12 Dissertation-Year Fellowship Awards. The fellowships carry a stipend of \$10,000 and full payment of tuition; recipients of these awards may also apply for grants of up to \$1000 for research expenses related to the dissertation.

Twelve doctoral candidates received awards for the 1988-89 academic year: Erma Lawson, sociology; Viju Mathews, metallurgical engineering; Samir Nandy, mining engineering; Ruth Rowles, geography; Eric Silberhorn, toxicology; Donald Tilton, mechanical engineering; Lauren Bowen, political science; Susan Campbell, biochemistry; Chong Chen, electrical engineering; James Dunn, entomology; Rebecca Eller, education; and Donald Good Jr., crop science.

"This initial group of fellows represents a large number of disciplines and is testimony to the breadth of excellence in UK's graduate programs," says Roselle. "We are proud that the University has been able to provide further impetus to the careers of these promising scholars."

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Faculty Awards Reach New High of \$52.6 Million

Grants and contracts to UK faculty reached a new high of \$52.6 million in fiscal year 1987-88. These are funds from federal, state and extramural agencies for projects to be carried out by the faculty. Private gifts and grants are not included in this amount.

Of the awards received, \$36.6 million was for research projects, \$6.4 million for instruction, \$8.3 million for public service, and \$1.3 million for other types of projects.

These external funds are an important measure of the quality of the re-

search efforts of a university because the funds are awarded on a competitive basis, nationally, which requires the faculty member and the research to be evaluated through stringent review processes. UK is ranked in a class of the top 45 public institutions and the top 70 of all institutions in the United States.

Dr. Wimberly Royster, vice president for research and graduate studies, says, "The faculty's success at attracting extramural support for their research has been a tremendous asset in attracting high-quality graduate students to our institution. It speaks very well for the faculty that they are able to successfully compete with research institutions throughout the nation for these awards."

In the past ten years, external funds awarded to UK faculty have risen from \$31.2 million to the present \$52.6 million.

Four UK Researchers Receive NIH Development Awards

Three associate professors—Mark Gillespie, Jack Olson, and Robert Yo-
kel—from the University of Kentucky College of Pharmacy, pharmacology and toxicology division, and Assistant Professor Subbarao Bondada, in the Department of Microbiology and Immunology, have received five-year Research Career Development Awards from the National Institutes of Health. The grants will go to support salary, benefits and research during this period.

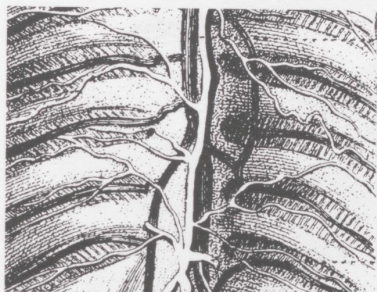


Dr. Gillespie received his approximately \$250,000 award from the National Heart, Lung, and Blood Institute of the NIH. Gillespie is researching the biochemical cause of pulmonary hypertension with emphasis on the role of polyamines, organic chemicals found in every body cell which seem to be essential for normal cell growth and differentiation.

Dr. Olson also received his award from the National Heart, Lung, and

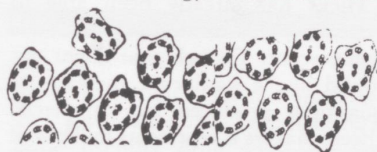


RESEARCH BRIEFS



Blood Institute. His approximately \$235,000 will enable him to focus his present research on understanding mechanisms essential for the development of hypertensive vascular diseases. Olson's research may lead to novel drug therapy that would interrupt or reverse pulmonary hypertension and possible systemic hypertension.

Dr. Yokel intends to use his \$235,000 award from the National Institute of Environmental Health Sciences of NIH to continue his research into the toxicology of aluminum and



the treatment of aluminum toxicity. Yokel is interested in how the aluminum in food and water and in pharmaceuticals gets into the body and, in turn, how it produces toxicity. His work will also further clarify the role aluminum may play in the cause of Alzheimer's disease. Evidence suggests that the element accumulates in selected regions of the Alzheimer-diseased brain.

With his approximately \$250,000 award, Dr. Bondada plans to continue his studies on the immune responses of older animals. In his current work, Bondada, who is also an associate of the Sanders-Brown Center on Aging, is focusing on the immune responses of older mice in order to determine how their systems deal with viral and bacterial infection. Bondada hopes to learn how to increase the effectiveness of this response, a discovery which could have implications for the human animal as well.



Growing Lettuce Without Soil: A Cleaner Bibb for the Table

Researchers at the University of Kentucky College of Agriculture are testing a newly developed breed of lettuce which seems to be especially suitable for hydroponic gardening.

"Hydroponics" is a technique in which vegetables, in this case lettuce, are grown in a water solution. Clean, tasty, nutritious lettuce is grown at UK in an environment where it never touches any kind of soil.

Hydroponics may be as promising for the home gardener as for commercial growers, according to Dr. Dean Knavel, a UK research horticulturist who has been working on hydroponics for years. All the gardener needs are some ten-foot lengths of four-inch plastic PVC pipe, some plastic tubing and a small pump. Shading is needed during hot summer months.

Knavel says that he developed a new line of bibb lettuce, but before he releases the new line he wants more information on how it does in hydroponics on a year-round basis. "So far," he says, "results of the experiments are encouraging. Taste tests show that this new line is comparable in taste and quality to that grown by traditional methods."

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"We grow our lettuce in troughs with running water which contains all the nutrient solutions the lettuce needs," Knavel says. "An obvious advantage to this technique is that you have a clean crop."

One big advantage to hydroponic gardening is the precision with which fertilizer can be applied. A gardener does not have to guess at amounts and hope that sufficient rainfall or irrigation will get the nutrients to the roots. City water can be used. If growers have well water, they should make sure it does not have a high salt content.

"Another advantage of hydroponics is that it saves water and nutrients," Knavel says. "You can use the same water and nutrients over and over. Then when you get through raising your lettuce, don't throw the solution away. Throw it on your rose bushes—it'll help the roses."

—Jerry Robbins

Shark Cheese

What do you get when you mix a shark and a gallon of milk?

What kind of riddle is *that*?

It's no riddle, it's research that Dr. Clair Hicks, cheese expert at the University of Kentucky's Agriculture Experiment Station, is about to begin. To be more precise, Hicks is going to use a very little bit of shark—a few enzymes actually—with a very large quantity of milk—a vat filled with up to 40,000 pounds of the stuff.

What he's hoping for is to reduce something called "agglutination," a natural process which reduces the amount of cheese that can be produced in the old-fashioned way. This process results from an antigen, an antibody in a milk cow's immune system, which attacks foreign bodies in both the bloodstream and in the milk.

That might be fine while the cow is walking around and needs protection from harmful bacteria. But it's not

so fine when the antibodies attack streptococcus bacteria cultures which cheese makers put into huge milk vats on purpose to make cheese.

"There are all kinds of streptococcus bacteria out there," Hicks says. "Some are bad. Some are good. Cottage cheese makers add about four percent of the good bacteria to ferment the milk to get the cheese. The antigen just clump onto these bacteria like they do the others."

That "clumping" creates long chains of cells which form a sort of net which slowly sinks to the bottom of the vat. As the chains sink, they trap something called "casein," the major protein in the cheese.

"As the chains sweep out the casein, they lower the solids at the top of the vats," Hicks says. "When the milk coagulates, we have lower yield at the top and a lot of useless sludge at the bottom. The sludge is not suitable for cheese, buttermilk or anything."

When the agglutination process is severe, a whole vat can be lost, Hicks says. Even when it is less severe, there is still a loss in both quality and quantity of cheese produced.

Hicks' research has been aimed at reducing the size of the "nets" formed during agglutination. By using cultures of "good" strep bacteria, he already has been able to break the chains from perhaps 150 cells each

down to about ten cells.

"By dramatically reducing the chain size, we reduce the amount of bacteria falling to the bottom of the vat, which reduces the amount of sludge," he says. "This means extra protein remaining in the milk, which increases cheese yield and improves the quality."

Hicks has already been able to improve yields by one to one and a half percent. Though that might not sound like a significant increase, at quantities produced by commercial cheese makers it represents millions of dollars.

But where does the shark come into the picture?

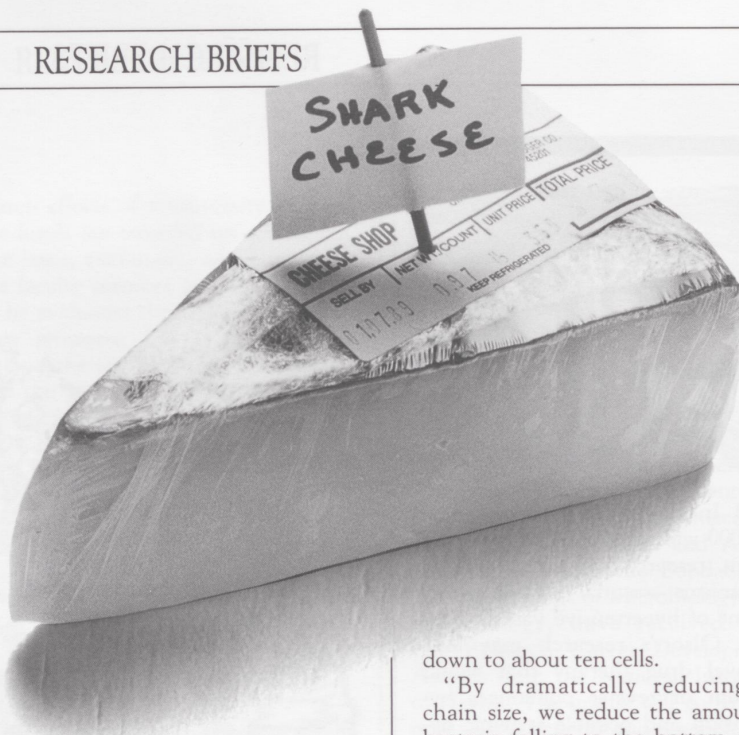
"We're planning to use enzymes from the dogfish, a small, voracious kind of shark, to help break those chains down further from the ten cells we've achieved so far," Hicks says. "We hope to break them down to one or two cells."

The principle he is testing is based on the cold-blooded nature of these sharks which inhabit colder parts of the ocean. The enzymes from the fish's pancreas act at cold temperatures to help break the chains, and then will deactivate by heating during the cheese-making process.

This research will be supported by a new \$88,600 grant from the National Dairy Products Board.

—Jerry Robbins

(Sources for Research Briefs include *The Ambassador*, The University of Kentucky College of Agriculture *NEWS* and *Spatula*.)



RESEARCH

Results

In the spring of 1982 the first issue of *ODYSSEY* Magazine was published. Given the nature of research and the years it can take to progress from point A to point B, *ODYSSEY* has generally featured projects at their inception. Now, in this new column, we want to go back and take a look in each issue at a project we have featured and tell you of the progress that has been made. Sometimes the results will be astonishing, sometimes they will seem like small steps—but all are contributions to new knowledge and thus signify progress.

The project discussed in this first column was featured in our first issue in an article titled "Marijuana: Innocuous or Harmful?" It is the nature of research that it is never complete; it always raises other questions to be studied. But through research we continue to learn and to progress. We hope you will enjoy this process with us.

—The Editor

Drs. Richard Clayton and Harwin Voss have been fighting a friendly drug war—between themselves—for more than a decade, and each is finding new ammunition in their latest data set.

The two University of Kentucky sociology professors are in the final stages of a ten-year nationwide study of chronic marijuana use among men aged 30-40. Their sample of 2,510 U.S. males was drawn from a Nixon-era Selective Service list released to them by H.R. Haldeman just two months before the draft board closed shop. Of that sample, 1,941 subjects were interviewed in both the initial 1974-75 survey and in the 1985 follow-up, a response rate of approximately 75 percent. The researchers note with pride that because this is a highly mobile segment of the population, their response rate was all the more respectable. "Chronic" use was defined as daily or weekly for five or more years.



Richard Clayton



Harwin Voss

In discussing their work, Clayton and Voss don't always agree on what should be done about the drug problem, but they point to some revealing findings from their research. "The more heavily involved with marijuana," Clayton notes, "the less likely they are to report a negative effect. Long-term cigarette and alcohol users say, 'Man, this is really bad for me.' Marijuana is a unique drug in that sense. The more you use it, the more

you think it does good things for you. It may be that the principal effect of the drug is short-term memory loss, so you can't remember when you were lying face down on the floor."

Voss lights another menthol cigarette and chuckles at Clayton's half-serious explanation, emphasizing that a better reason may be the "mysticism" surrounding the drug. "It's an accepted drug among a certain segment of our population," he says. "If you stratify our population by age, say, talk to an audience of retirees, they put marijuana right on a par with heroin. They see no difference. High school kids would laugh at that because they know they're different drugs."

This study suggests that the focus on drug abuse in the elementary schools may be somewhat misplaced. Clayton argues that tragic cases of youthful drug abuse should be considered the exception rather than the norm. "The idea that marijuana use has seeped into the elementary schools, that that's where it starts, comes from taking a few kids who've tried it at that age, and extrapolating this sample to the entire population. It simply is a figment of our imagination and our fears. The average onset of marijuana use hasn't changed much in 15 years. It's still somewhere around 15-16."

Voss adds that "one of the things we can say with real assurance is that use of marijuana is very tightly linked to age. There is a very real difference experientially in that young people in this society are very likely to have at least tried marijuana. Their parents haven't. The 18 year-old who hasn't smoked pot is more atypical than his peer who has."

Disentangling the causal nexus surrounding pot use and the tendency to move on to harder drugs is something of "a chicken and egg question," Clayton admits. "It's not pharmacological. It's a social and relational

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RESEARCH *Results*

phenomenon." Voss also cautions against causal judgments about progressive drug abuse. "There's nothing about the drug itself or the pharmacology of it, but when you look at this data set, you find almost no one who has used cocaine who hasn't used marijuana."

Drug abuse may have its roots in far more common forms of "deviant behavior," Clayton suggests. "Most of the kids who have tried marijuana have also previously tried cigarettes and alcohol. For anybody to make an assertion that the age of marijuana use has crept into the elementary schools means one of two things. Either cigarette and alcohol use and experimentation are occurring earlier, or the gap between trying one and trying the other has narrowed considerably. The data just don't show that either has happened."

Although the direction the causal arrow points is uncertain, what is clear from their research is that pot smokers are more likely to engage in other "deviant behavior." According to Clayton, "You can say that people who are heavy marijuana users are more likely to have multiple divorces. We don't know whether the marijuana use is a coping response after the divorce, whether the marijuana use led to the divorce in the first place or whether the spouse was upset because the guy really wasn't very good at keeping a job." Clayton adds that the pot users surveyed were also more likely than non-users to have trouble maintaining a career.

Voss adds drunk driving, shoplifting and cohabitation to the list of "deviant behavior" more common among pot smokers than among the general population.

Clayton and Voss believe their study suggests a strong link between pot use and pulmonary dysfunction, although the causal arrow is again uncertain. "We have difficulty saying chronic marijuana use causes pulmonary dysfunction," Clayton says, "because most of the heavy marijuana users are also heavy cigarette smokers. They are also much more likely than their non-marijuana-smoking

cohorts to smoke cocaine." Confounding as those variables may be, they do reinforce the study's profile of pot smokers as "deviant" individuals who run high health risks.

Clayton and Voss agree that pot smoking has drifted into a perverse kind of respectability among a segment of our society, creating an aura within which the dealer often operates, Clayton observes, "as if he were an MBA from Harvard. It reflects in an economic sense some of the same things that are going on in the legitimate economy. And why shouldn't we expect that? You have minimum overhead and maximum profit potential."

The increasingly streamlined nature of the pot culture in some ways makes prosecution more difficult, Voss argues, since marijuana use is so ingrained in the baby-boom generation. "That's why I'm convinced, as Richard isn't, that using criminal sanctions for marijuana is simply inappropriate."

Clayton rises to the challenge. "Are you saying we should legalize marijuana?"

Not exactly, Voss elaborates, but since more than half of those in the age group surveyed have smoked pot, "it is pure foolishness to pass a law you can't enforce, that makes criminals of half the population. Maybe we should control it with age limits like we use for alcohol and cigarettes."

"Well," Clayton begins, smiling wryly at Voss's smoke, "we know good and well that cigarettes are the major health-care cost factor in America."

Their affable drug war is on again, and perhaps their data is more stringently examined for all their disagreements. What is certain from the work of these jovially combative social scientists is that—given pot's link to deviant behavior and to divorce, and given marijuana's cloudy-but-present place in the pulmonary dysfunction nexus—research on this drug will continue. ■

—Gary Pierce



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Back Cover Photo:

University of Kentucky researcher Betty Sisken and her colleagues have found that low levels of electrical stimulation appear to speed regeneration of nerve tissue and improve circulation by increasing growth of new blood vessels. See article titled "Faster Healing with Electricity," page 14.

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