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One of a series of torsos by UK artist John
Tuska is formed with hand-made paper
and then covered with graphite. More
about Tuska's work can be found in the
Odyssey article entitled *From Rags To
Artistic Richness*.

ODYSSEY

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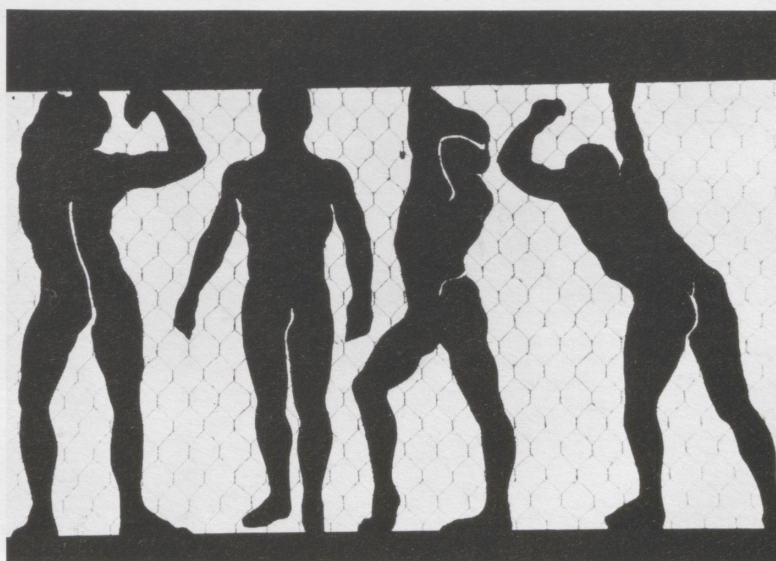
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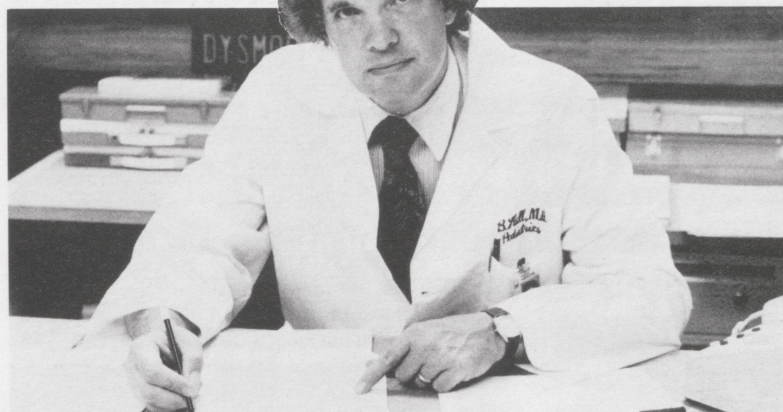
THE DIAGNOSTIC PURSUITS OF A DYSMORPHOLOGIST

On his way to one of the genetic counselling clinics which he established in six Kentucky towns, Dr. Bryan Hall studied photographs of a deformed stillborn infant. In a few hours he would talk with the parents. They would want to know what disease had caused the death of this child and of two others, previously stillborn. The diagnosis would not be easy. Hunched in the back seat of the compact car, driven by genetic counselor Barbara Bowles, Hall reread the case file and looked again at the distressing photographs.

"Getting to see the pictures is very informative," he frowned. "However, rather than decrease the possible number of disorders which might be present here, the photos suggest even more."

With impressive accuracy he is able to diagnose common and rare diseases by looking at patients. Sometimes the symptoms are obvious, other times almost undetectable—"a crease in the wrong place, a hair pattern not where it should be."

A 43 year-old Kentucky physician recently returned from California, associate professor of pediatrics at the University of Kentucky College of Medicine, Hall has another more precise identity—he is one of the nation's few



Dr. Bryan Hall

dysmorphologists, expert at diagnosing genetically related disease from physical abnormalities. With impressive accuracy he is able to diagnose common and rare diseases by looking at patients. Sometimes the symptoms are obvious, other times almost undetectable—"a crease in the wrong place, a hair pattern not where it should be." Once he makes a diagnosis, Hall explains the disease to parents or other relatives in counselling sessions which sometimes are painfully difficult for everyone.

"It's a tremendous responsibility for a family to deal with genetic counselling," Hall said. "It has its advantages, but also its disadvantages. One couple will come in for counselling and you will have to say to them, 'This is a severe genetic disorder. You have a 25 percent chance of mental retardation.' The couple will say, 'That's it—no more children.' Another couple with potentially the same disorder will never bother with counselling and have two perfectly normal children because they were lucky. Like the other couple, they had a 75 percent chance for normal children."

"Under certain circumstances, counselling can be a very negative factor. A family is referred for counselling, comes in and is totally devastated by the information. They don't know what to do

with it and they wish they hadn't heard it. That's why we prefer counselling to be the family's idea. Counselling is not always as beneficial as we think it is. It always requires sensitivity, knowledge and the right kind of follow-up counselling."

Hall's reflections flow from 17 years of experience, much of that time in California, where as associate director of the Birth Defects Center at the University of California-San Francisco, he operated 13 outreach clinics. With a federal grant and assistance from the Commonwealth he is setting up a similar network of genetic counselling clinics in Kentucky.

After an hour's drive, Hall accompanied by Bowles, and medical student Les Beisecker, is met at the entrance of a county health department building by two public health nurses.

A few minutes later Hall is chatting with an amiable local woman whose granddaughter has just returned to the town after corrective leg surgery at an eastern hospital. The woman's normal sons are afraid to marry because their children could inherit the disease that caused the girl's problem. She has photographs of members of her family and information suggesting to Hall, as he works through a careful generational

"pedigree" of the family, that inbreeding has occurred. Typically, inbreeding is not flagrant. In an established community

In an established community where families have remained for generations, a marriage 75 years ago between a man and a woman who did not know they were cousins could have produced in their offspring or in distant descendants a deformed infant.

where families have remained for generations, a marriage 75 years ago between a man and a woman who did not know they were cousins could have produced in their offspring or in distant descendants a deformed infant. Without the sort of detection Hall provides, the cause might remain a mystery and a continual source of anxiety.

As Hall completes the charted family history, the woman observes that defects in other members of the family had been attributed to Polio. "Polio got blamed for a lot of things," Hall replies. "It deserved to get blamed, but sometimes that diagnosis was wrong." Putting aside his pencil, he studies the pedigree and begins to explain to the woman how normal and abnormal characteristics are inherited through dominant and recessive genes.

"You may carry a single abnormal recessive gene and it will not adversely affect your health or physical features," he tells her. "But if you mate with someone who has the same abnormal recessive gene, 25 percent of your offspring are at risk of getting both recessive genes and manifesting the disease." In one obvious way her sons

can reduce the risk. If they seek wives outside the community, Hall says, they will dramatically reduce the likelihood of their combining the same abnormal recessive genes. Seemingly relieved, the woman gathers her family photographs—except for a few Hall keeps for his file—and leaves.

In a way, Hall's career began with some casual advice as to the value of photographs of patients for a young physician. Hall's father, Paintsville pediatrician Dr. Lon C. Hall, stimulated his son's interest in the outer manifestation of disease by observing that he wished he had kept photographic files of his patients.

"When I was getting my pediatric training in Louisville," Hall said, "I used this old camera to take pictures of interesting patients. It didn't focus well up close, but from a distance it was fine. The only patients that you didn't have to have close, detailed shots of were those with gross physical abnormalities—people with birth defects."

Noticing that his medical colleagues knew little about birth defects or their consequences as the children grew older, Hall sharpened his abilities. By 1967, as a first year pediatric resident, he was the in-house expert on birth defects at Louisville Children's Hospital.

"Anyone who does something that other people do not do and does it well has a tremendous ego feedback system created," Hall said. "As I was talking with families and doing counselling, I found the families dearly appreciated the information that had been so hard to obtain. Then, as I was able to diagnose these rare disorders, my colleagues would ask me for unofficial consults."



From Louisville Children's Hospital he proceeded to a fellowship at Great Ormond Street Hospital for Sick Children in London, then to residency with the Wessex Regional Hospital Board in England, and in 1968 to a staff pediatrician's position at David Grant U.S. Air Force Hospital in California. There he started a genetics clinic. In 1970 he joined the Dysmorphology Unit at the University of Washington School of Medicine's Department of Pediatrics. At Washington he found a mentor who profoundly influenced his life.

"When I decided on academic medicine and on genetics in particular I went to Washington on a fellowship," Hall recalled. "At that time most genetic research was biochemical and I didn't want that orientation. I was able to do purely clinical work with Dr. (David W.) Smith. He was a fantastic gentleman and a scholar. He combined simplicity and science like no other man I have known."

Two years later Dr. Hall moved to UC-San Francisco, where he remained for nine years—"an extremely busy and very exciting time." When he felt he was "running out of steam" he took a sabbatical study leave with Dr. Jurgen Spranger in Germany. Back in California to finish training some of his genetic Fellows, he realized that "the next ten years would be like the previous ten. I needed a new challenge." So after nine years of helping run the largest genetic service in the U.S., he left California for Kentucky.

Kentucky needed the genetic services Hall could provide, but he also had personal reasons for responding to UK's job offer: Simply put, he found he was one of those Kentuckians who inevitably return. "When I think about it," he said, "I see I always felt guilty about leaving. My Kentucky upbringing prepared me for this type of work because I learned to talk on any level with sincerity, honesty and concern."

One of the public health nurses introduces Hall to the couple whose infants have been stillborn. Hall knows that this couple's future children will risk a "clearly lethal genetic disorder." Without destroying hope he must explain to them their prospects as parents. They recount their experiences, then listen to his explanation.

Hall tells the couple that he is not yet able to provide a diagnosis, but in spite of their bad luck they theoretically have a 75 percent chance for the birth of a normal child. "We don't know what is wrong with your babies—something," Hall says. "We don't know what it is. Somewhere down the line we're going to know what's wrong. It will be a slow process." He offers a grim assurance—"It doesn't look like this situation is compatible with life for the baby"—and carefully raises the question of termination of the pregnancy if the disorder is detected in the fetus: "To take it back one step further, I have no idea how you feel about terminating or aborting the pregnancy . . ." In this way, gently and sympathetically, he suggests that the shocking discouragement they have experienced need not prevent parenthood.

Understandably, the couple wants to know why they were not warned by other physicians of the risk they faced. "A lot of doctors are not trained in genetics," Hall explains. "Genetics only became an area of medicine from the standpoint of training physicians in the last ten years." They seem satisfied with the explanation and indicate their willingness to undergo testing to determine the nature of their problem.

A few days later Hall was delivering his weekly diagnostic slide-show at a lunch hour meeting of pediatric interns and residents at the UK Medical Center. The teaching he does in the Medical Center is highly valued: He received the Pediatric Faculty Teaching Award for 1981-1982.

Each of his slides showed some abnormality or combination of abnormalities indicating the presence of malformations. For pediatricians the identification of features—often almost unnoticeable, sometimes masked by other, more evident abnormalities—is a crucial skill. The failure to recognize these symptoms could mean unnecessary physical impairment or death for a child. He showed a photograph of a child whose unusually formed chest bore an extra nipple and whose pectoral and shoulder muscles were underdeveloped. He told the young pediatricians that this underdevelopment often was associated with a poorly developed arm and hand on the same side.

This piecing together of medical evidence would be less critical if laboratory tests could provide verification, but testing does not always tell a doctor which syndrome the patient has. The most powerful microscopes may show chromosomal abnormalities, but even magnification may fail to reveal the secrets of the tiny gene. This persisting uncertainty explains why in his teaching Hall emphasizes "pursuit"—the intense analysis of symptoms, tenacious desire for exact diagnosis. "You must have great diagnostic pursuit," he said. "I could never tolerate not knowing. I tell my students that pursuit is as important if not more important than observation and factual knowledge." His students are grateful. One pediatric intern said the detailed observations Hall encourages will help him to "make specific diagnosis rather than simply describing the patient as having multiple congenital anomalies."



A vague diagnosis—"multiple congenital anomalies"—carries with it a note of dismissal. Hall offered one example. He has diagnosed, treated, and counselled in about 10 cases of Pierre Robin Anomaly. These are children born with lower jaws which are so small that, in the fetus, the jaw will not support the tongue. The tongue falls back, obstructing closure of the roof of the mouth, causing cleft palate. At birth the tongue also covers the breathing passages a "life threatening" situation. The child's ears will be low on the neck. The physician may assume from its "very unusual appearance" that it "is abnormal all over and may be mentally retarded."

By recognizing the symptoms and understanding the development of a child afflicted with this anomaly, a physician may start the child on the path to normal growth and health; by failing to understand the syndrome, the doctor may consign the child to unnecessary problems and even death.

In fact, if the position of the tongue is corrected, this supposedly abnormal child, Hall said, will "grow into a perfectly normal child, just take off." By recognizing the symptoms and understanding the development of a child afflicted with this anomaly, a physician may start the child on the path to normal growth and health; by failing to understand the syndrome, the doctor may consign the child to unnecessary problems and even death.

For all the weighty implications of his work, Hall remains relaxed and personable. He is an active researcher who has published 62 papers, and his approach to research also is relaxed: "When I see an interesting situation not seen before I write that up and publish it." It is hard to imagine him working in a laboratory. Obviously he enjoys caring for patients, and he brings to these duties a blend of clinical interest and sympathy. "You know how interesting people are in their normal state," he said. "Well, they are even more interesting in their abnormal state . . . But I don't define people as normal or abnormal. I just think of them as interesting."

—Michael J. Kirkhorn

One of the most coveted research grants in academe is awarded by the National Institutes of Health. The grant is called a Research Career Development Award and offers recipients five years to devote exclusively to research. Two such recipients are in UK's Thomas Hunt Morgan School of Biological Sciences—John Rawls and David Prior—and they offer us some insight as to the significance of such an award for a researcher.

SEARCHING FOR BIOLOGICAL SECRETS AMONG THE ODISIOUS SLUG AND THE LOWLY FRUIT FLY

University of Kentucky Associate Professor David J. Prior knows what it's like to juggle teaching and research, and he remembers times when he would squeeze research into the hours after his children were in bed.

That changed when the 38-year-old biologist received a five-year Research Career Development Award from the National Institutes of Health, one of the most prestigious grants made to young researchers.

Prior and UK officials worked out an arrangement that freed him of teaching responsibilities and allowed him to devote more time to his research on how the brain controls behavior. The grant pays his salary.

NIH looks at "whether your research is at the point at which it really needs a boost," Prior says. "If you could get out of the classroom, would it take off?"

Using the slug, which he personally finds "odious: the most offensive creature ever to crawl upon the earth," Prior hopes to find out how the nervous system controls behavior.

Prior not only got out of the classroom, he got out of the country, spending a year studying neural control of terrestrial mollusks in the laboratory of the distinguished zoologist John Treherne at Cambridge University in England.

Last year he returned to his own lab in UK's Research Facility No. 3, equipped with sophisticated devices for observing, monitoring and recording the activity of a specific terrestrial mollusk—the garden slug.

Using the slug, which he personally finds "odious: the most offensive creature ever to crawl upon the earth," Prior hopes to find out how the nervous system controls behavior.

Most of us know that nerve cells in our brains control how we move our arms by causing the muscles to contract. But we also know that the response to stimulation varies.

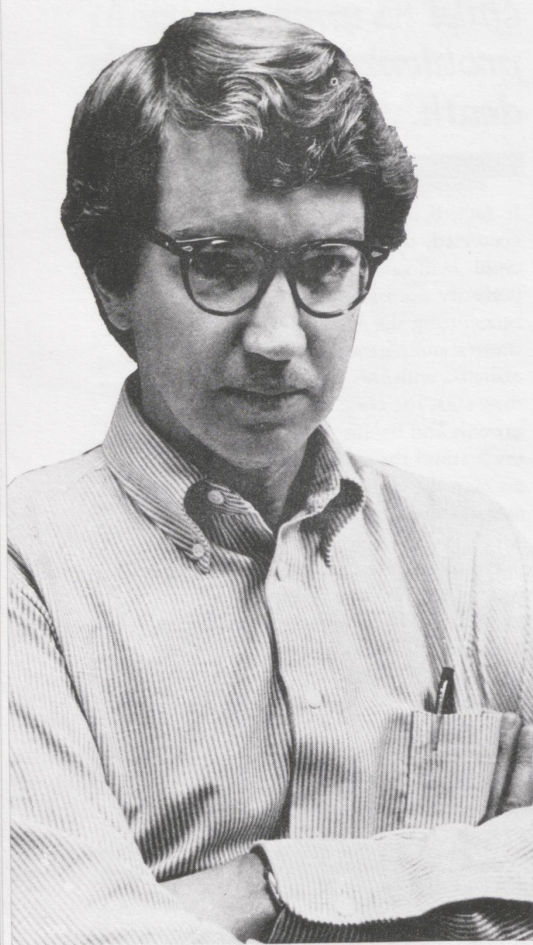
If someone pokes us in the ribs, we might cry out, or giggle and twitch or merely jerk away. Why, Prior asks, when the stimulation is the same, does the response vary? The same question can be asked about moods: if someone says there's a party, one night we might feel like going and another like staying home.

"We can't analyze 'mood,' so we use less complicated animals. We used to call them simpler, but they're not simpler. They have fewer nerve cells, only a few thousand compared to the millions in the brain of a cat or a man. And the slug's brain cells are relatively large, which makes it easier for researchers to pierce them with slender glass electrodes.

"Like a cat—or a man—a slug is capable of associative-type learning.

"Their brains are capable of complex behavior that we don't usually associate with that sort of thing," Prior says. "We can look at the behavioral response and ask how that behavior changes."

Prior is studying the slug's water regulatory behavior, in which each response is modified to help the mollusk regulate its water balance. For example, if a slug's water level is down, it won't eat dry food because it loses moisture when it



DAVID PRIOR

eats. Rehydrate the slug and it will eat. It will drink when dehydrated, but stop when its water balance is restored, and it will close down its breathing hole when dehydrated to avoid evaporating water from the lung into the air.

"We understand how the brain detects dehydration, but we don't understand how the nervous system provides signals to turn on 'thirst,'" Prior says. "We may have a shot at finding out."

"(Slugs) can serve as a model system for a broad range of other animals . . . to varying extents I believe that (what we find here) will affect water balance in humans."

Prior finds it encouraging that after only three-and-a-half years of research, he is at the same level as researchers studying vertebrate systems, since that research is considerably older. All the data to date indicates that the common feature in vertebrates and invertebrates is increased concentration of salt in the blood, Prior says.

"When I have to justify my research, I think that I'm adding to our basic knowledge about life systems—how the nervous system functions," he says. "From that basic body of knowledge some will go this way and study aging or epilepsy or go that way and study strokes. People will take different tangents."

"We lay the groundwork, and others say 'we can apply this.'"

Prior began focusing on the neural control of behavior as a Sloan Foundation fellow from 1977 to 1981. His most recent grant from NIH has primarily meant "more thinking time."

"When you have a three-lecture course, you're either giving or preparing for lecture every day of the week but

Saturday. You say, 'It's almost 10, I've got to get there . . . what am I going to talk about tomorrow . . . I've got three students to see this afternoon,'" he says.

"To do research, you have to know you have all three hours off this morning. You can do stuff you would ordinarily do at home or in the library at night."

It's not that Prior dislikes teaching. In fact, he finds it "ironic that I have something that I enjoy that I'm freed of."

The course he likes best is "Biology for Poets," his name for the service course for non-majors, because it is "a truly spectacular opportunity for the students and the instructor. Rather than the hard-core column of stuff you jam into (an upper-level course), this has a different goal: to give people some basic concepts and put them in a palatable form so they can understand them."

His aim is to encourage students to think about the world. Without understanding biology, he says, people cannot make rational decisions about the most controversial issues in our society, such as whether to allow experimentation with recombinant DNA; whether to legalize euthanasia; to permit certain birth control methods; or establish test tube baby clinics.

"There's a lot going on in the public arena, and if one has no sense of basic biological principles . . . without some understanding of what's going on . . . one can't make decisions."

For him, the great scientists are those who have the flair and creativity to take their research beyond the collection of basic scientific observations. Prior tries to encourage that kind of creativity in his students.

As a starting place, he doesn't approach teaching as a matter of requiring students to memorize a text. Instead, he wants them to exercise their curiosity. "It strikes me that biologists have an advantage. It's something everybody is intrinsically interested in—how their bodies work."

Scientists "always keep our eyes open for potential," he adds, noting that what begins as a casual observation may produce valid scientific data.

Prior loves the seashore, but it's much more than a playground for him. Since his research involves mollusks, which include octopuses, squids, snails and slugs, his summers at Woods Hole, Massachusetts' Marine Biological Laboratory, provide fertile ground for observation and experimentation.

Someday he might like to live elsewhere, perhaps on the coast, but now he is pleased to be at UK, where his research facility is "very good," and where he has had the chance, along with other young scientists, to build the program in the School of Biological Sciences.

He has secured generous grant support, due in no small measure to his ability to express himself articulately. Drawing on his own experience in writing successful grant proposals and his review of a number of other scientists' proposals, he says the chief thing is for the principal investigator to write a proposal "so anyone can understand it."

"You can have excellent ideas and be able to prove them, but if you can't sell them, you won't get funded." By the same token, "a good writer can't make it unless there's good science."

Prior has demonstrated that he can do both.



Searching Continued

JOHN RAWLS

University of Kentucky's John M. Rawls did what many Americans who get to live in France might do: he spent a lot of time sightseeing, learned a little about French wines, and he even gained a few pounds.

But Rawls did something else during his year abroad that few can imagine: he learned to clone a gene—the basic unit in inheritance.

Strasbourg is known for its beautiful setting in French-German Alsace and for its cuisine. Few know that the city is also home of an international research center where 60-70 scientists each work on a different aspect of gene cloning.

In his year at the lab, Rawls, assistant professor in the School of Biological Sciences, learned recombinant DNA technology: placing designated genes into bacteria and viruses, cultivating, harvesting, and chemically analyzing the cloned gene.

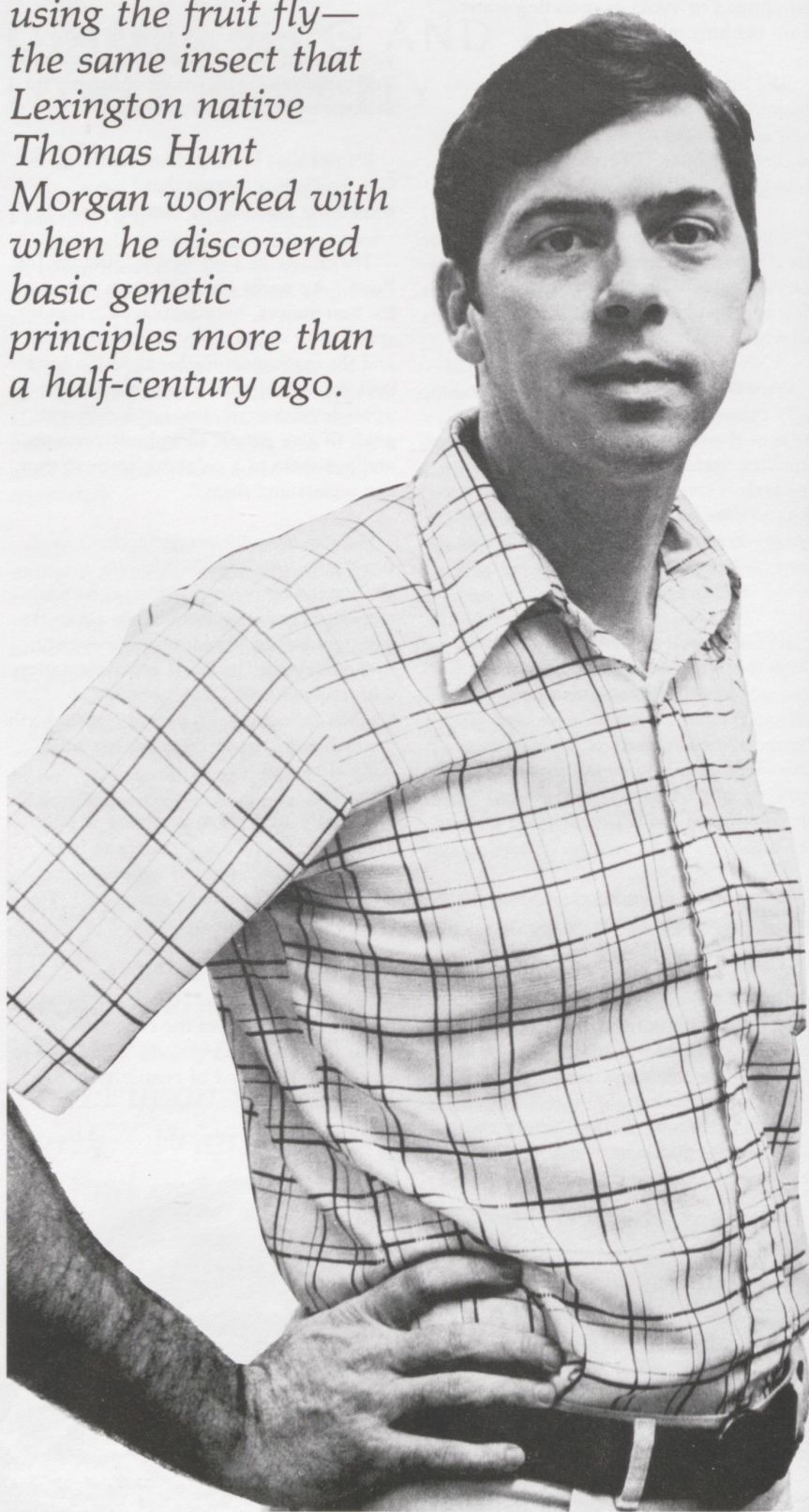
Although the basic technology is fairly widely used, the advantage to being at the Laboratoire de Genetique Moleculaire des Eucaryotes of the Centre Nationale pour Reserche Scientifique (CNRS) was that Rawls had "access to all these people: virtually every technique (of gene cloning) that might be useful is being practiced here," he said in a telephone interview while still in France.

Back in his lab in UK's No. 3 Research Facility, Rawls will work on cloning two other genes in order to use them as tools to understand the mechanisms of heredity.

Rawls's research has no direct clinical application. "Curiosity is the justification," he says. "The reason I go into the lab every day is to satisfy my basic curiosity."

He adds wryly, "I wouldn't say curiosity is an important national objective." But he says his area of

Rawls pursues his basic genetic studies using the fruit fly—the same insect that Lexington native Thomas Hunt Morgan worked with when he discovered basic genetic principles more than a half-century ago.



research is "very basic, and while not directly applicable to medical, legal or social objectives, the things that I and other people discover lead to an understanding of basic processes like inheritance.

"My contribution is to the knowledge of society of itself and of the world around it."

His research is significant enough that the National Institutes of Health awarded him a five-year Research Career Development Award which pays his salary and frees him from teaching responsibilities.

"Its purpose is to enhance the research potential of promising investigators by permitting them to spend more time on research, freeing them from administrative and teaching responsibilities that they always have to deal with," said Maureen Harris, director of the Research Career Development Program for the National Institutes of Arthritis, Diabetes and Digestive and Kidney Diseases.

"It's a very prestigious award for promising investigators."

Now midway through the grant, Rawls pursues his basic genetic studies using the fruit fly—the same insect that Lexington native Thomas Hunt Morgan (for whom UK's School of Biological Science is named) worked with when he discovered basic genetic principles more than a half-century ago.

Rawls credits Morgan's description of a particular fly wing mutation with leading him into his specific area of research. But Rawl's approach is far more sophisticated than Morgan's could be. Rawls does his studies at the molecular level, something not possible in Morgan's day.

Using techniques developed in the last five years, Rawls analyzes the chemical nature of the processes of inheritance, asking how genetic material replicates, recombines and mutates.

The fruit flies that occasionally escape from the racks of glass jars and tubes and flutter about Rawl's lab look no different from those that hover over the ripe fruit at home. What makes them such valuable experimental subjects?

The processes that go on with this fly are essentially indistinguishable from what goes on in humans . . .

"The processes that go on with this fly are essentially indistinguishable from what goes on in humans and animals, but they don't have an easy little wing with which to dissect biochemical processes," Rawls responds.



Over the last two years, the 36-year-old scientist has isolated mutants in order to study the different steps of a metabolic pathway or system. He has found that the pathways consist of different genes produced in synchrony. What do those genes have in common that permits them to be controlled at the same time?

He theorizes that there are regulator elements which control the activity of the pathway genes. "Genes are quite separate and yet operate in unison, so there must be signals from some to others."

He uses two approaches. The first, which he describes as making "an educated guess," involves looking for mutations of the regulator by looking at mutations of the fruit fly wing itself. That is basically the approach used by Morgan—a systematic process of observation, description and conclusion.

The second is more complex. Rawls thinks he has found a biochemical way of asking the genes in a specific metabolic pathway, "what turns you on and off?" By cloning out certain genes, that is, by isolating the structure in its pure form, he says he can use those molecules to "fish around" for the regulator.

His research has had some intriguing spin-offs. In doing structural analysis of mutants, Rawls also has been looking at a phenomenon that only recently has come to light—transposable genetic elements.

Scientists have always thought of genes as being static, unchanging material, but recent research shows they are part of the genome, the molecule that contains genetic information, and that portions of the DNA—the main carrier of genetic information actually move around.

"This gives us a different perspective on mutation," Rawls says. "Instead of thinking that mutations are things done to us by other things (such as X-rays), we now feel that many and most mutations are an aberrance of processes that occur normally within us."

It could be that X-rays and other stimuli believed to have mutagenic effects are actually triggering the aberrance rather than causing the mutation, he said.

Absorbed in his research, Rawls says he has all but forgotten about teaching. Yet he looks forward to going back to teaching because he feels that he has matured and will be a better teacher.

The experience in Strasbourg has been happy in other ways. He says it has been a lot like a sabbatical. "I've learned a whole new area, a whole new set of techniques, without teaching classes, administering grants. One just doesn't have the ability to expand that way without time to get away and indulge oneself.

"This year I've had all the advantages."

—Maria Braden



FROM RAGS TO ARTISTIC RICHNESS

The medium is cast paper.

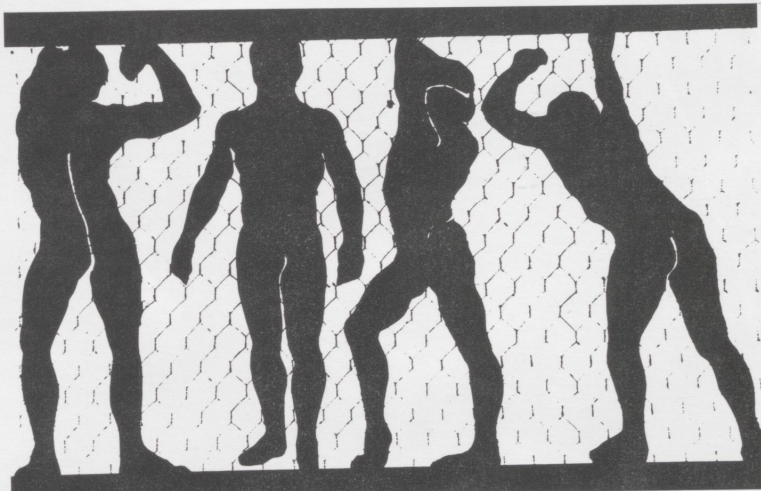
With his fingers John Tuska pushes and pats sodden pulp into the depressions in a plaster mold, blotting up excess water with a sponge.

"I start with rags. Students bring them in, I scrounge them. Cotton, and when I can get it, linen."

He helps himself to another handful of pulp from a blender. "The blender shreds and batters it, the water breaks it down more. Color comes from color in the cloth. I don't use any chemicals . . ."

"[His] steady growth as an artist has been one of the certainties of the art community I have observed for 20 years. His creative vitality, applied with thought and knowledge, has produced work of substance and beauty—whether the pots of his early career or the 'high art' of the present."

Sarah W. Lansdell, Art Critic
The Courier Journal



A portion of a screen Tuska has made of 12" high wooden figures.

Behind him in this cluttered studio stands a rack of more molds, made of plaster, coated with shellac, and now awaiting casting.

Tuska pushes pulp against the borders he has clamped against sides, top and bottom of his mold. When a thin layer covers everything, he blots the whole and leaves it to dry.

When dry, this "water leaf" paper, now formed into a relief picture, will lift easily from its mold. Tuska will size it with graphite, maybe add a bit of color, then burnish the surface until it looks and feels like metal.

More often than not, the work is a human form—head, face, torso. "Most of my work is figurative," Tuska says and he means figurative, literally.

A powerful example is the graceful, dynamic human figures, printed from hand-cut linoleum blocks on a sheet of paper six feet long—illustrations Tuska made for a limited (75 copies) edition of Swinburne's "On the Cliffs" published last year by the Margaret I. King Library hand press.

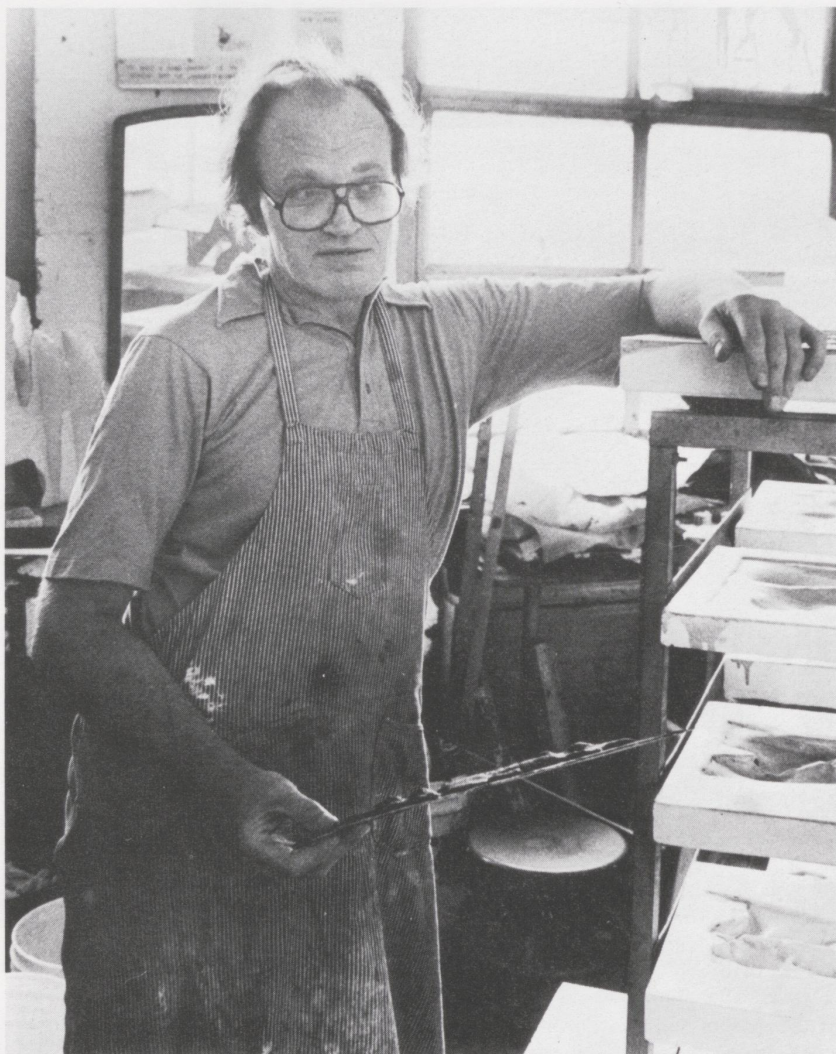
Or the screen he made for his home—64 wooden figures 12 inches tall, each cut by hand from hardwood and set in a wooden frame about seven feet tall and 32 inches wide.

Or his "Torso Series" in cast paper which last November won him the Museum Guild Purchase Award—top prize—at the Mid-States Art Exhibition in Evansville, Ind.

Tuska's drawings are mostly figurative—drawings in pen and ink, pencil and mixed media that make up many of the shows (eight in the first half of 1982) to which this prolific artist is continually being invited to contribute.

Tuska works, speaks and moves with energy and enthusiasm, qualities he believes are crucial to the creative life. Since school's end, when he began a year's leave from teaching under a University of Kentucky Research Award, he's completed some 40 molds (plaster over sculpted wax or clay), experimented with combinations of materials for papermaking and tried alternative ways of finishing surfaces.

Left—Tuska pen & ink study of torsos.



"John's interpretation of the human form is bold and strong—delicate and quietly lyrical in any medium he pursues. Whether the form emerges from clay or flows onto paper from his hand, it is through very hard work, his unique and positive outlook and his incredible talent and energy to see beyond and within, that he is consciously able to extract and consistently produce work that exists quite simply on its own."

Irwin Pickett
Director of Visual Arts Ky. Dept. of Arts

Also he has prepared a drawing show for the blood bank gallery in Lexington, shipped off another show (15 paper pieces, the largest three by four feet) to the Showcase '82 at Louisville (one of 16 artists chosen from among 115 contenders), exhibited his cast paper at Gallery 545 in Lexington, and assembled drawings and cast-paper works for yet another exhibition at Transylvania University's Morlan Gallery.

"Sometimes," Tuska says, "I feel like a driven person."

He arises at 5:30 and begins work soon afterward in the big, Queen Anne-style house he shares with wife Miriam or in his studio at the UK Reynolds Building.

"Ideas keep popping into my head. I jot them down in a notebook. Or I draw them. The other day I woke up at 3:30 with an idea for a drawing. I got up, went downstairs and drew it."

Tuska's vitality, so abundant in his work, charges his whole life. Perhaps it is a legacy from his gypsy grandfather who emigrated to America from Slovakia and died here, at the age of 107. Tuska's father followed the grandfather to the U.S. and went to work in the Pennsylvania coal mines. John, at 12, was apprenticed to an upholsterer.

"I've worked continuously; my survival depends upon work. The creative person has to work, and to be extroverted. Work requires drive, energy, persistence. And work generates new ideas."

Tuska, trained as a potter (MFA from New York State College of Ceramics), came to Kentucky to teach ceramics at Murray State. At Murray he "discovered I didn't know how to draw" and he proceeded to teach himself. One looks at the lovely pencil portraits of his two young sons—or at any of his drawings for that matter—and sees immediately his mastery. He keeps "drawings going constantly" in a pocket or bedside notebook. Soon, because "I don't like to repeat," Tuska had moved past the potter's wheel, experimenting with clay in new forms and at the same time "always looking for new materials."

From clay he created "Genesis," a high relief stoneware wall commissioned for the 18th floor of UK's Patterson Office Tower, in 1969. He missed its unveiling;



Tuska and his family flew to Italy that year, his sabbatical, where he worked in another medium at the bronze foundries of Rome.

His sculpture, ceramics and drawings are on display in a number of public collections, among them the city hall at Deauville, France; university buildings at Vanderbilt and Xavier, New Orleans, and museums in Wichita, Kansas, Champaign-Urbana, Illinois and State College, Pennsylvania, as well as the

Institut di Belle Arti, Rome and St. Hubert's Church, Lexington.

But it is in this new medium he has discovered that all Tuska's talents appear to come together—sculpture, drawing, painting, color, mechanics. Tuska has taken paper further, probably, than anyone else ever has.

Curiosity, as always, was his motive. In 1978 he attended a UK workshop in papermaking. "I just wanted to make

drawing paper," he says.

Then, "I began to wonder what would happen if you molded paper." After that, "What if you added color, or graphite." One wonders if Tuska has now taken paper to its—Tuska's limit. "I hope not," he says. "I'm playing with some other ideas."

"He shapes his personal visions—bodies in motion, for instance—through the screen of antique art works. In our minds differences in time vanish, images merge in a unique ideal. John Tuska expresses the intriguing complexity of modern man."

Mme. Helene Lassalle, Curator
Museum of Modern Art,
George Pompidou Center, Paris

The Smithsonian Institution last year invited him to open a file of personal documents in its Archives of American Art. "I've sent them photographs, newspaper clippings, letters and papers, samples of materials, drawings, receipts, sketches," he says.

"Yes, it is a very great honor."

Also collecting Tuska material is the Georges Pompidou Center at the Museum of Modern Art, Paris. If Tuska had to choose, today, his best work for either archivist, which would he select?

"My current best? Well, I think my current best is yet to come." He points to a big hand-lettered sign taped on a studio wall. *NON BASTA UNA VITA*, it says. *ONE LIFETIME IS NOT ENOUGH*.

—Betty Tevis

DRUGS: DESIRABLE & UNDESIRABLE

Three drugs—Valium, Librium, and Meproamate—accounted for 89 percent of the 214 million prescriptions for psychotherapeutic drugs filled in the United States in 1973. Thirty-eight percent of these were new prescriptions; 62 percent were refills.

Many of those chronically taking Valium in large doses may experience undesirable side effects including severe depression and dependency.

Valium—the trade name for Diazepam, an anti-anxiety drug—is one of the drugs being studied by Drs. William Martin and Laura McNicholas, two University of Kentucky pharmacology professors, whose research is aimed at developing methods to identify and separate the properties of sedative, hypnotic and anti-anxiety drugs that produce desirable and undesirable effects. Phenobarbital, Secobarbital, Oxazepam and Lorazepam will also be tested and compared with each other as to the severity of their abstinence syndromes, and the effects that occur when the drugs are mixed with alcohol.

Several series of experiments are being done to study the effects of these drugs' properties. The first is a dose-response experiment using dogs and rats. The researchers are studying the animals' behavior after they are given the drugs in varying amounts. Dependency is also being studied by using the dose-response animal experiments.

"This type of research is particularly important when you realize that 10 to 20 percent of the population of the United States will have serious problems with sleep at some time in their lives, and will commonly visit their doctor for sleep or calming medications," said Dr. Martin.

However in many other cases, visits to the doctor may be unnecessary, according to Dr. Robert Straus, chairman of Behavioral Science. "People often take over-the-counter drugs or visit their

doctors for aches and pains or transitory sleeplessness that I would call 'the normal stresses of daily living.' Most people who visit a doctor expect to be given medicine for whatever complaints they may have—it is a very pervasive expectation in our society. Somehow patients do not think they have gotten their money's worth from a doctor's visit unless they are given some kind of medication, and their family and friends support this expectation. The media are partly responsible. Advertising tells us to take something for every minor ache or worry or 'trouble' getting to sleep. And the ads stress that medications should be 'strong' and 'act quickly.' Of course some people are more susceptible than others to these messages, but the connection exists. This type of atmosphere also creates pressure on doctors to prescribe medicine in an attempt to fulfill the patient's expectations."

But for those with serious sleep problems, there is still the problem of undesirable side effects from medication. "There is hardly a chemical that doesn't have both desirable and undesirable effects," Straus said. "The goal for both the physician and the patient is to maximize the desirable effects and minimize the undesirable or so called 'side effects.'"

Dr. Robert Straus



The medications being studied by Martin and McNicholas "frequently produce unwanted or undesirable side effects along with the desired effects," Martin said. Some of the more common among these effects are:

1. When taken in slightly greater than the prescribed doses they impair motor performances, causing drowsiness and a slowing of reaction time.
2. The drugs can change feelings—Some people with sleep disorders are prone to depression and the drugs create feelings of well being. As a result, some people begin to take the drug to achieve this feeling rather than reserving it for sleep problems.
3. Patients can become tolerant to and physically dependent on the drugs, needing constantly larger doses to produce the desired effects. When the patient does not receive that daily dosage he or she may suffer from an abstinence syndrome.
4. When these drugs are taken with other sedative hypnotics or alcohol they produce severe depression.

"However, simply because a drug may interact with alcohol in an adverse manner should not preclude prescribing the drug in appropriate circumstances," McNicholas said.

"There are a number of reasons that people misuse medications," Straus said. "And one that is commonly overlooked is poor communication between the doctor and the patient. Perhaps the patient did not clearly understand how he or she, was supposed to take the medicine. Because good communication skills are crucial, universities are beginning to put more emphasis on them and requiring medical students to take communication classes.

"Another reason exists because of the biological differences in patients. Behaviorally and biologically people react differently to varying amounts of medication. Most medication is prescribed in what is said to be a normal dosage for most people; however, what is normal for one patient may be too much (or too little) for another."

For example, aspirin, Straus said. "Everyone knows you take two aspirins. Why? Because the advertising and the directions on the bottle tells us so. At some point it was decided by the manufacturers that two is the normal dose to bring about the desired effects. However, two aspirins may be too much for some people, and cause gastritis and bleeding of the stomach. The same is true, when you are looking at sedatives, such as Valium. What maybe be a normal dose for some, may be too much for others, causing dangerous drowsiness or feelings of depression that outweigh the desired anti-anxiety or muscle relaxing effects.

"This is certainly a very real danger when you examine the additive effects of sedative drugs with alcohol," Straus said. "A person who normally can take two or three drinks without experiencing intoxication may appear drunk after only one drink if he or she is at the same time using a sedative medication. In any case, sedatives like Valium should not be taken with alcohol, because they often produce dangerous drug interactions.

"There is even research that shows there are differences in the way the body uses drugs at different times during the day or month or as people get older. So not only must individual reactions be taken into account, the doctor and patient must allow for the changes during the menstrual cycle and the life cycle, itself. As people get older there are changes in the rate that medications are absorbed, metabolized, stored and excreted. Older people metabolize many drugs more slowly, store them longer and excrete them more slowly. In other words, the drug will remain in the person's system longer, allowing more time for undesirable interactions with other drugs. This risk is compounded because older people have more health problems and tend to take more medications than younger people.

"Besides dosage, interaction and additive effects, people may misuse or appear to be misusing drugs because they



have become dependent, that is, they usually require increased doses of the drug to produce the desired effect.

"No one knows why some people become physically dependent on drugs and others don't," Straus said. "This appears to be a combination of biological vulnerability or sensitivity that may be genetic in nature and factors of exposure to or experience with using a drug. People who are vulnerable won't become physically dependent if they never or rarely use the drug and some people can be heavy users of drugs like alcohol without becoming physically dependent. We can't explain psychological dependence either. Although these are some psychological traits that are often observed in people with a drug dependence, many people have the same traits without becoming dependent on a drug. At the extreme, there are people who have a propensity for being overly dependent in general—on medicines, family, doctors, employers.

"Dependency is a very normal human trait. Babies and some older people are more dependent. In middle life we tend to be less so.

"Most people who regularly come home and have one or two alcoholic drinks to relax are displaying a kind of dependency, just like having one or two cups of coffee in the morning before you begin work—because it makes you feel and function better. It is a form of dependency because if the alcohol or coffee is omitted, the individual will miss it and probably won't feel quite right. But there are generally no problems with such dependency, unless it begins to interfere with functioning or health."

However when people use drugs to the degree that they become dysfunctionally dependent, they have achieved a "disbalance between the desirable effects and the undesirable side effects," Straus said.

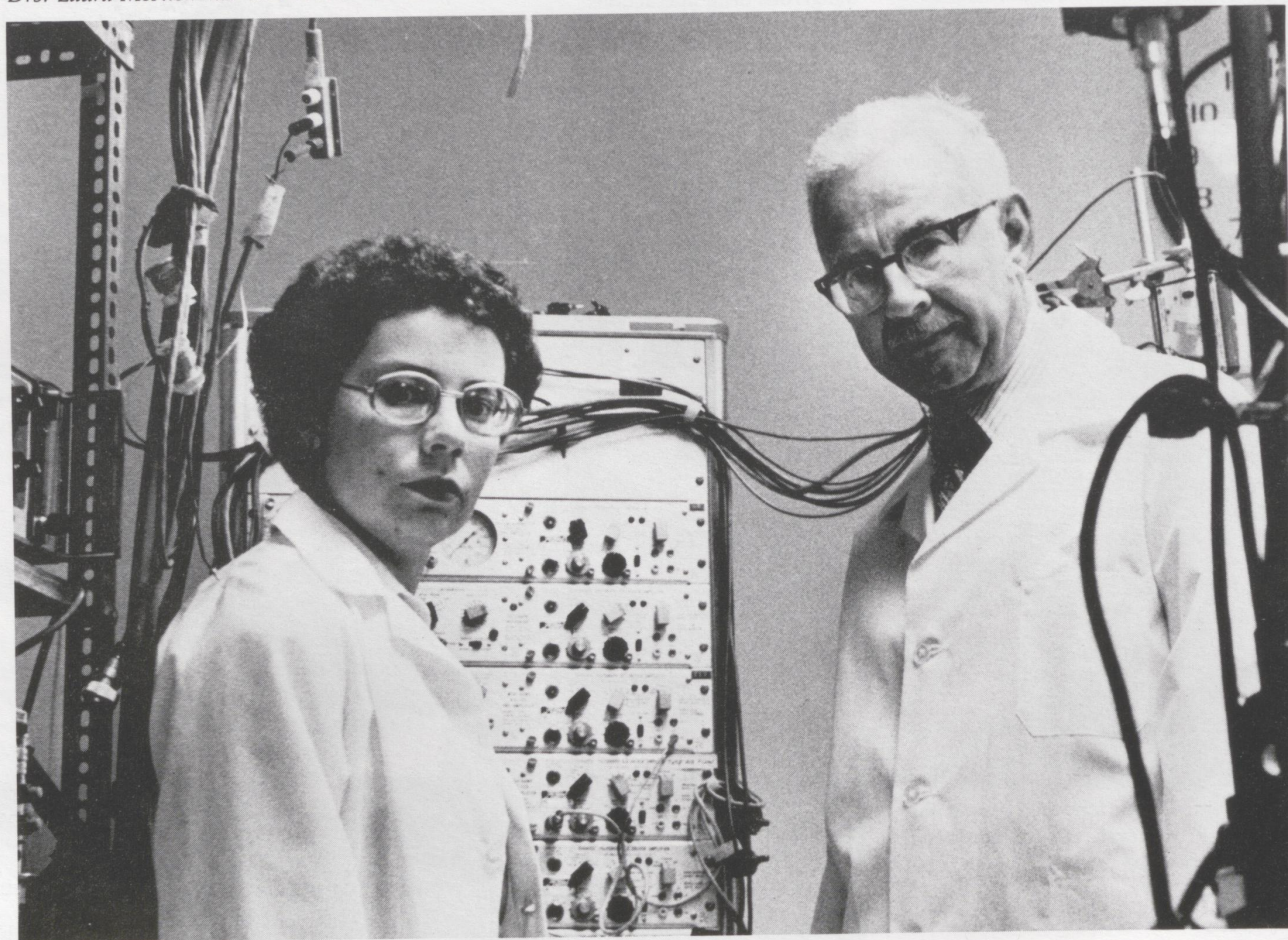
"Such dependency is characterized by the need for more of the drug to achieve the desired effect—an increased tolerance, the use of the drug interferes with function and a preoccupation with making sure the drug is easily accessible extending to protection of their access to supply," Straus explained.

Although, the identification and separation of the drugs' properties alone will not stop people from developing psychological dependency or keep them from misusing the medication, the research will provide insight into the physical dependency cycle and aid in the future development of drugs that will produce less undesirable side effects.

"The research we are doing will eventually help in the designing and identification of better drugs that will be more selective in their action," Martin said.

—Tawny R. Acker

Drs. Laura McNicholas and William Martin





A Prescription for Success?

She glanced at the clock; ten til ten. Almost time for her first appointment of the day and it was an important one. She shifted uneasily in her chair and tried to shrug off the clammy feeling that was rapidly spreading from the armpits of her silk blouse. Then came the familiar prickling sensation along the back of her neck.

It always began like this, she thought—the vague feeling of unease, the clamminess, the pin cushion feeling (as she had come to refer to it), and then the numbness and paralyzing fear that at one time masked her talents and kept her in middle management jobs.

But no more. She glanced around her office, her gaze stopping for a moment on the small Chagall print then coming to rest on the silver cache on her desk. Carefully, she opened the lid and removed a slim, monogrammed pill case.

"Ahhh." It was an involuntary sigh, and she guiltily glanced around to see if anyone had heard. But of course there was no one to hear or see as she lifted the two pale blue tablets to her lips.

Later that evening at a cocktail party, she was smiling and chatting confidently with D.W. Arneau, chairman of one of the largest product conglomerates in Atlanta, about an account she desperately wanted to land. The conversation ended with him asking her to call and set up a presentation. Flushed with the pride of achievement, she quickly wound her way to her

husband's side with the news. He gave her a quick hug and offered to get her another glass of Dom Perignon to celebrate. She hesitated, and then declined—it had been two hours since she had taken two 10mmg. Valiums and the doctor had warned her about mixing medication and alcohol.

And she was someone who could follow orders well. Since his caution, she never had more than one glass of chilled white wine with lunch so as not to interfere with her morning dosage, and never more than two cocktails in the evening. Her friends and colleagues were often amazed at her ability to stop after so little libation but she didn't dare tamper with the beneficial effects of Valium. After all, she would never have been in the position of director of accounts at Atlanta's largest public relations firm without those pale blue pills.

For years, everyone had known she was talented, but they had also known she couldn't cope with the pressure of strenuous deadlines, deliver coherent presentations; she could only offer ideas.

But that had changed and changed quickly about four years ago when she had begun dating her future husband and he suggested she see a psychiatrist. Within a month the doctor had prescribed an occasional Valium with intensive therapy sessions. It had worked, everyone remarked upon the change. And gradually she was promoted. She wondered what others must have thought was responsible for the changes and, to key people, she mentioned that she was in therapy—after all, in certain circles, it was even considered chic.

"Are you ready to leave?" her husband asked. His voice brought her back to reality. She quickly surveyed the other guests to see if any of them had noticed her inattentiveness. "Yes, I was just admiring the view," she said.

She was tired that night after the party but everything kept whirling around in her head. What was wrong? Nothing she could pinpoint—but something. She reached into the drawer of the bedside table, took two Valiums and tried to think of nothing—a cool, black nothing—as she waited for the calming effect of the drug to lull her into sleep. Her last thought as she slipped into the cocoon of sleep was that she must remember to keep her appointment with the doctor. It was the second time this week she had rescheduled. "I really don't have time tomorrow either," she thought, "but I must keep this one." Her cache of Valium was empty.

The next morning as she rode a cab across town, she cursed the doctor's refusal to refill her Valium prescription until she kept her appointment. She had long since resigned herself to the fact that it was the Valium, more than the therapy sessions, that had helped her come to terms with her life—why couldn't the doctor accept it? Some people, like her, just couldn't get well—of course, she would never admit it to anyone else—she didn't even like to think about it—but she didn't think she could function without Valium.

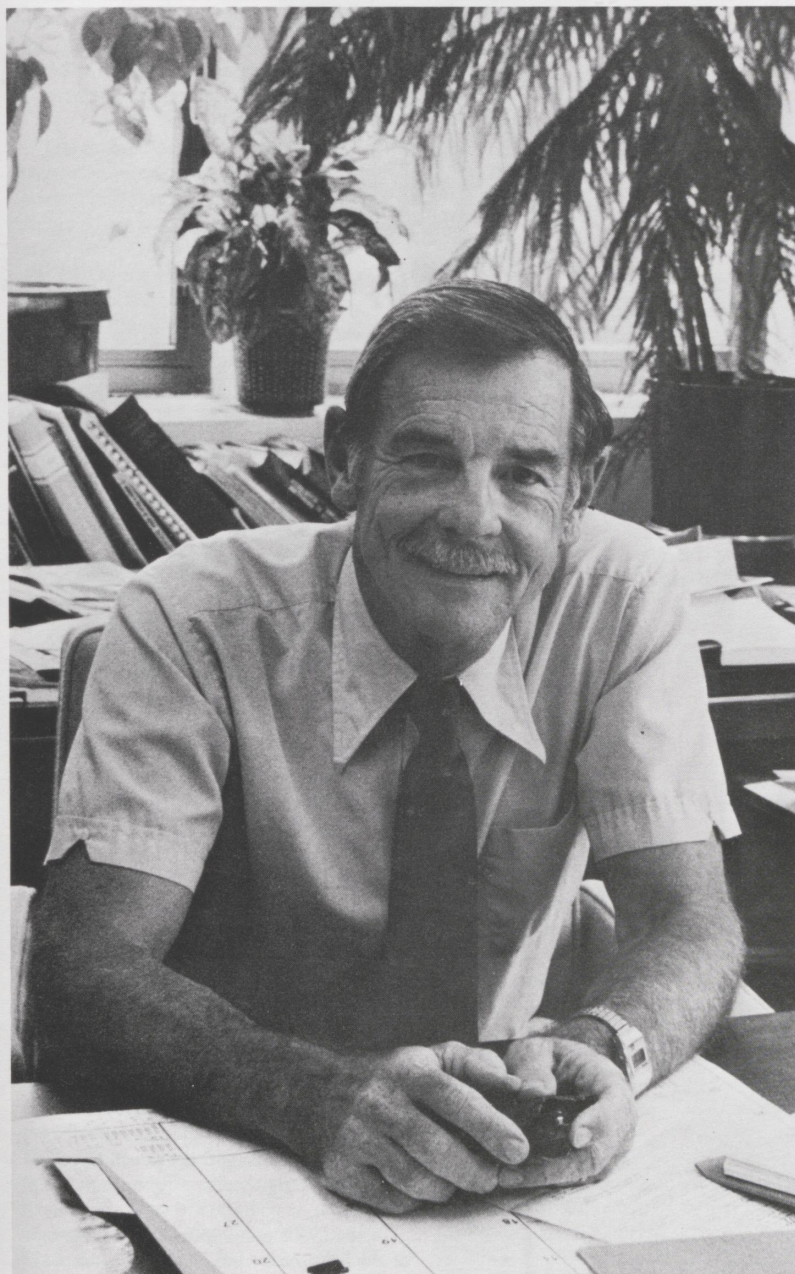
At one time she was alarmed that she seemed to be taking larger and more frequent doses in order to feel relaxed, but she always followed the doctors caution about mixing it with alcohol. She also remembered his caution about becoming dependent on the sense of well being the medication created.

"But I guess I shouldn't worry too much," she thought as she entered his office, quickly checking her purse to see that she had her internist's prescription for Valium, just in case.

—Tawny R. Acker



THE HOMOGENIZATION OF APPALACHIA



Dr. Tom Ford

1961—The “War on Poverty” had just begun. It was the indoctrination of a nation. Photos of dirty, raggedy wide-eyed Appalachian children stared from the evening news, and their fiercely proud, but bewildered parents wondered aloud to reporters what all the fuss was about.

Appalachia had become the darling of the media. Stories perpetuated by journalists and novelists alike described people living in abject poverty such as was thought only to exist in third world nations.

The country was aware that Appalachia was different, and the nickname, “America’s final frontier,” seemed appropriate. It became evident that the social services available in nutrition, health care and education were not adequately meeting the needs of this group of people. President John F. Kennedy started programs like VISTA, aimed at providing assistance for the country’s underprivileged, particularly those in Appalachia.

Certain regions of Appalachia were and are different from the rest of the country and they may require specialized services, Dr. Tom R. Ford, director of the UK Center for Developmental Change said. “For this reason we are interested in studying the data available from 1958 and 1976 census surveys and determining the changes in household patterns, such as the gender and average age of the head of the household, education, the number of members in a household and average income.”

Ford, Dr. Jim Brown, UK sociology professor, Tom Arcury, Center for Developmental Change research associate and Dr. Julie Porter, research assistant, are involved in the project.

“Most people,” Arcury said, “still draw their impressions about Appalachia from local color writers, comic strips or outdated information.”

Ford and Brown previously collaborated on a survey of southern Appalachia published in 1962. The results included selected characteristics of a 1958 household survey based on interviews conducted by the Survey Operations Unit of the University of North Carolina, Chapel Hill. Although this study divided the population into three residential areas: metropolitan; smaller towns and cities and; rural areas, the present study will examine only metropolitan and non-metropolitan areas.

"Especially in the very rural areas of Appalachia, the inhabitants' life styles in the 1950s centered around family relationships," Brown said. "Puritanism was an important part of their value system; hard work, for example, was emphasized. A class structure, based on their values, was found to be important even in small, isolated neighborhoods. During the 1960s the area had a heavy loss of population as thousands migrated with their families to work in midwestern industrial cities and especially in southwestern Ohio. The faltering economy of the 1970s stimulated a return of some of these migrants to their native communities in Kentucky as well—household size and makeup were changing and more women were working outside of the home, for instance."

Brown, an Appalachian native, is one of the authors of "Mountain Families in Transition" an in-depth study spanning four decades, which followed the people of an isolated mountain area, Beaver Creek, in Eastern Kentucky as they struggled to adapt to the increasingly dismal economic and social conditions of their environment. While working on the Beech Creek study, Brown spent months in the neighborhoods studying the cultural and social organization of the residents, first in the early 1940s and later in the 1960s.

"Certainly one of the most important patterns, perhaps the most important one, in Eastern Kentucky's culture is familism, that is, the emphasis on the family and familistic patterns in virtually all cultural



Tom Arcury

and social patterns," Brown said. "As in the greater American society, the primary kinship group is the conjugal family (husband, wife and immature children) but in Eastern Kentucky the extended family is much more important. The extended family is not a formal, institutionally defined set of kin. Rather it is an informal group of families formed from the relatives of the husband and/or his wife, the membership of which is determined by many factors—geographic location, class status, land resources, etc." Brown calls these informal groups "family groups."

Brown points out that this concept of kinship is responsible for the clusterings of transplanted Kentuckians in industrial areas in parts of Michigan and Ohio. "One by one they would leave Kentucky and go to wherever their relatives had gone and settle near each other. All the members of a family group tended to

migrate, usually over a considerable period of time, to a particular city or area," Brown said. "They never forgot their roots. Come Friday, after the last shift, they would load up their families and head for Kentucky. Interstate 64 would be bumper to bumper to Kentucky and Sunday afternoon it would be the same way in the opposite direction."

At the time of the southern Appalachian survey and the Beech Creek study, the household usually had a male head who was the breadwinner and a wife who stayed home. However, the times they were a changing as both the 1958 survey study and the Beech Creek study noted.

In the 1940s and 1950s, the average age of the head of a rural household was a male 30 to 40 years old with an eighth-grade education. The main occupation in the rural areas was farming and the wives

did not work outside of the home. Parents tended not to live with married children, but to maintain a closely located, but separate household.

The 1958 data from the southern Appalachian survey Ford, Brown, Arcury and Porter are using as a comparison with 1976 data from the Census' Current Population Survey, is coming from the archives at Berea. Because the questions were worded differently on both surveys, the researchers are having the 1958 data recoded to fall into specific predetermined categories used in 1976.

The researchers expect that the national trends in living arrangements will be evident to some degree in rural Appalachia, but the amount of change and the implications for changes in services to the residents of the area are only speculations at this time.

"I think this study will show that Appalachia is different from the rest of the country in some ways, just the way Ohio is different than Pennsylvania, but not as radically different as some of the literature suggests."

The results will very likely confirm what the previous studies foresaw happening, according to Brown. The average age of the head of the household will probably have decreased because of the in-migration that occurred in the 1970s. There will probably be an increase in the number of single parent households, and in conjunction with this, an increase in the numbers of women as heads of households and who work outside the home. The average educational level of heads of households has probably increased; while the number

of members of households decreased. There are also probably a larger number of elderly people living in separate households and an increase in the number of unmarried couples living together.

"I think this study will show that Appalachia is different from the rest of the country in some ways, just the way Ohio is different than Pennsylvania, but not as radically different as some of the literature suggests," Arcury said.

Brown agreed. "From the time I became involved with the Beech Creek people, I saw some drastic changes over a period

of years. Families suddenly had gas, electricity and indoor plumbing. Black-topping the roads made travel to other communities a normal experience. Schools were consolidated and people started to shop and go to church in other places, not just the closest location. People could observe the progress taking place in other communities and began to change their own life styles."

Changes in life styles precipitate changes in the kinds of services that need to be offered. For example, if the study shows that many women are heads of households in single-parent families with

Dr. Jim Brown



young children, then the services offered by industry and extension agents will have to be altered to meet the single mother's needs, Ford explained. "Industry will probably have to make arrangements for day care facilities and extension agents will have to offer sessions on preparing quick nutritious meals, rather than an all-day session on canning."

Another recent phenomenon that the researchers expect to encounter is the single female parent that sends or gives her child to her parent, its grandparents, to be adopted. Perhaps with more support from social agencies, the single mother would not feel compelled to release her child into her parent's custody, Ford said.

The advent of more older people living alone in separate households may necessitate some additional or expanded services. The "Meal on Wheels" program that in some areas delivers balanced meals to older citizens or brings them to eat at the headquarters may need to be expanded or, in some areas, begun. A type of program that uses a network of daily phone calls to check on elderly persons may be necessary especially if the citizens live in isolated areas.

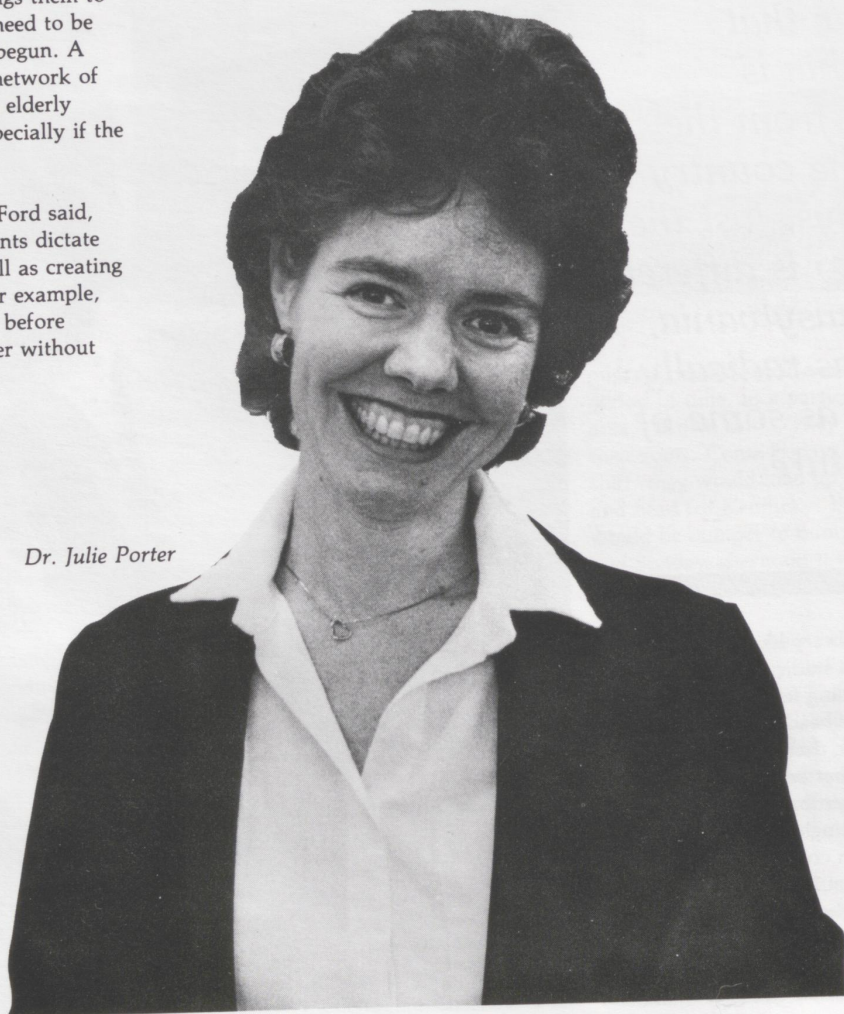
"You have to remember," Ford said, "changes in living arrangements dictate new laws and customs as well as creating markets for new services. For example, who ever heard of palimony before couples started living together without being married."

"The significance of this research is that it allows society to evaluate the adequacy of services being provided."

1982—The "War on Poverty" in Appalachia is at a standstill because the fight has become a nationwide struggle. The country's state of the economy has necessitated a rational return to the extended family living arrangements prevalent during the 1950s in Appalachia, while at the same time the rising divorce rate has made single parent households an accepted phenomenon in the most rural of Appalachian areas. How have the changes in living arrangements affected the fabric of Appalachian culture—the traditional family? Only time and research will tell if Appalachia is still the "final frontier."

—Tawny R. Acker

Dr. Julie Porter



A QUESTION
OF MIND
OVER BODY:

Can Humans Learn To Control Their Immune Responses?

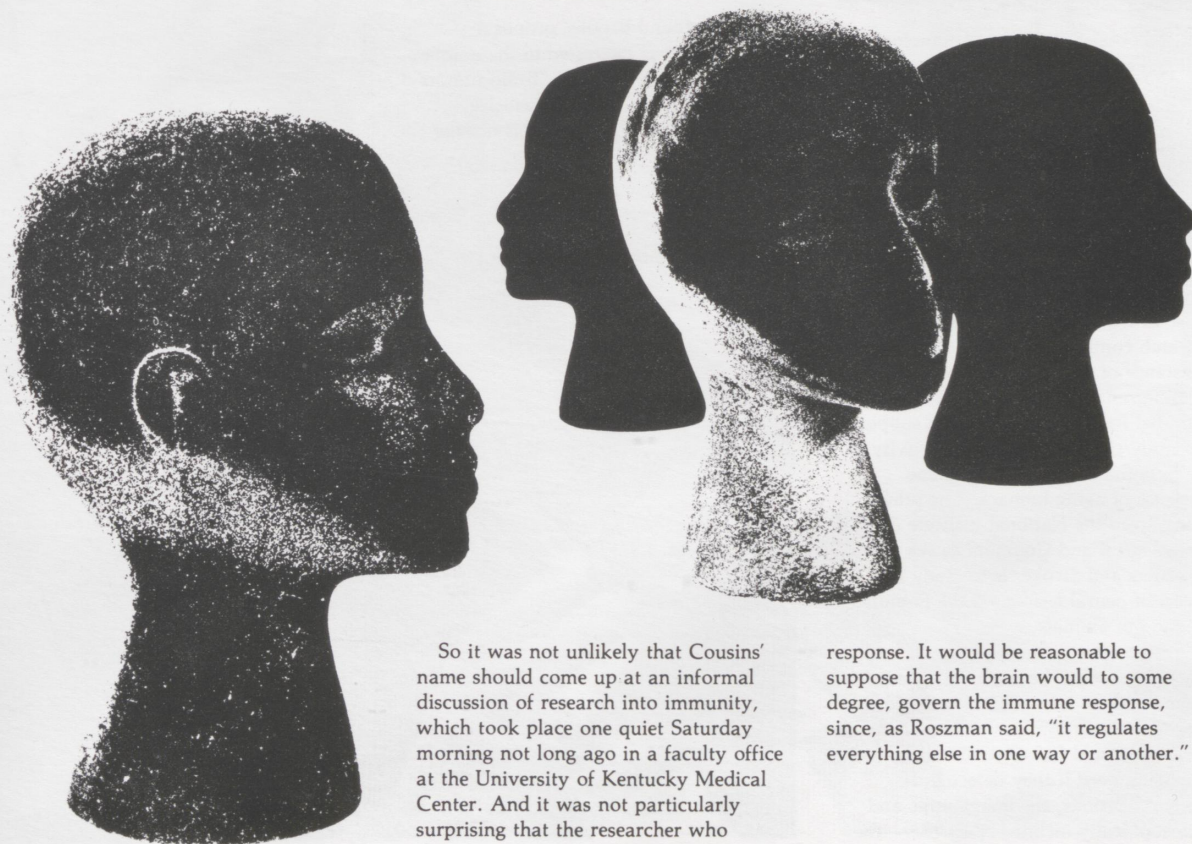
When Norman Cousins, editor of *The Saturday Review*, overcame a grave and potentially lethal disease by laughing at the movies of Charlie Chaplin and other film comedians, he impressed, among others, a lot of medical scientists.

Researchers did not universally dismiss Cousins' exercise in self-healing as a fluke or a fraud or just another improbability. They saw in the editor's experience proof of a traditional physician's maxim, that well patients do well: In other words, patients who maintain high spirits resist disease more effectively than those who submit or surrender. Cousins also strengthened the belief of many researchers who feel more and more strongly convinced that the mind—the workings of the brain—is instrumental in the resistance of disease.

mentioned Cousins was Dr. William Markesbery, director of UK's Sanders-Brown Research Center on Aging and one of the University's most rigorous scientific investigators.

Markesbery has been working with two other researchers—Dr. Thomas L. Roszman and Dr. William H. Brooks—on a sequence of experimental studies which have revealed important, if controversial, connections between the brain and the functioning of the immune system. They have experimented only on rat brains, but their findings may have considerable implications for humans.

So far, the UK researchers have shown that the brain “modulates” the immune



So it was not unlikely that Cousins' name should come up at an informal discussion of research into immunity, which took place one quiet Saturday morning not long ago in a faculty office at the University of Kentucky Medical Center. And it was not particularly surprising that the researcher who

response. It would be reasonable to suppose that the brain would to some degree, govern the immune response, since, as Roszman said, “it regulates everything else in one way or another.”

"The fascinating thing is the possibility that we may be able to use our brains in ways we never have used them before. This research conjures up a sense of an inner self. If we can scientifically explore an aspect of the inner self never looked at before we may be able to make a real contribution."

But, he observed, "most immunologists still feel that the immune response is largely autonomous." Putting it another way, Brooks, a neurosurgeon, said that immunologists tend to "want to see the immune system as a closed package."

The UK team's findings have met far less resistance from neurological scientists, who Brooks said, "know that the brain is all powerful." It is from this sense of the brain's power that the research continues—currently with the assistance of two National Institutes of Health grants. One grant is from the National Institute of Aging and supports the study of the effects of the activity of the hypothalamus on the immune response of aging humans. The other grant, from the National Institute of Neurological and Communicative Disorders and Stroke, is to study the effects of neural lesions on the immune function of animals.

Stirring not far beneath the surface of the methodical scientific investigations is another expectation—one which many scientists would feel uncomfortable discussing even if they detected its presence. Brooks, the imaginative and philosophically inclined researcher—the

team's designated visionary—put it this way: "The fascinating thing is the possibility that we may be able to use our brains in ways we never have used them before. This research conjures up a sense of an inner self. If we can scientifically explore an aspect of the inner self never looked at before we may be able to make a real contribution."

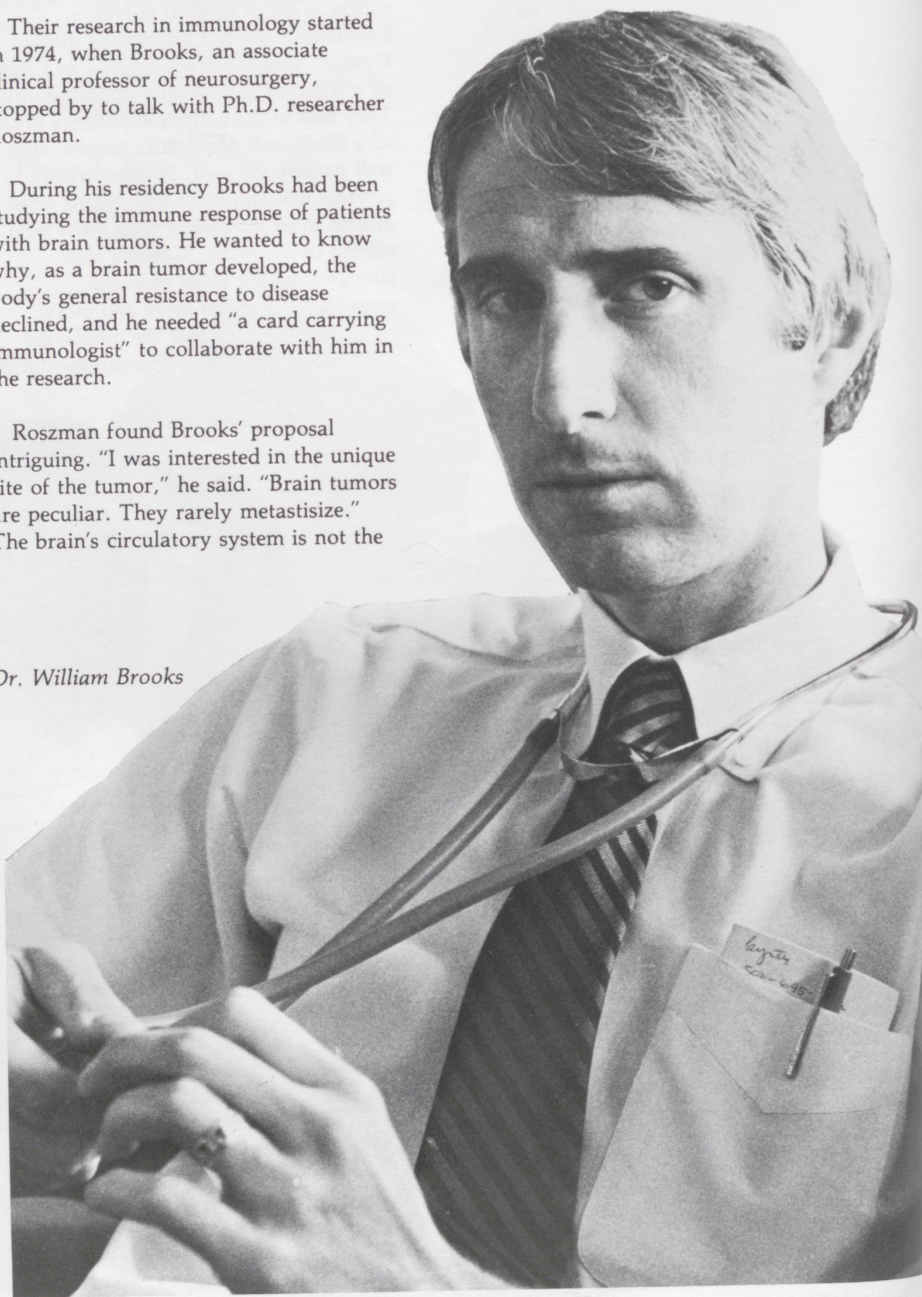
The long-term possibility, then, is that humans may learn to control their immune response. Determining the brain's influence over the immune response is one starting point.

Their research in immunology started in 1974, when Brooks, an associate clinical professor of neurosurgery, stopped by to talk with Ph.D. researcher Roszman.

During his residency Brooks had been studying the immune response of patients with brain tumors. He wanted to know why, as a brain tumor developed, the body's general resistance to disease declined, and he needed "a card carrying immunologist" to collaborate with him in the research.

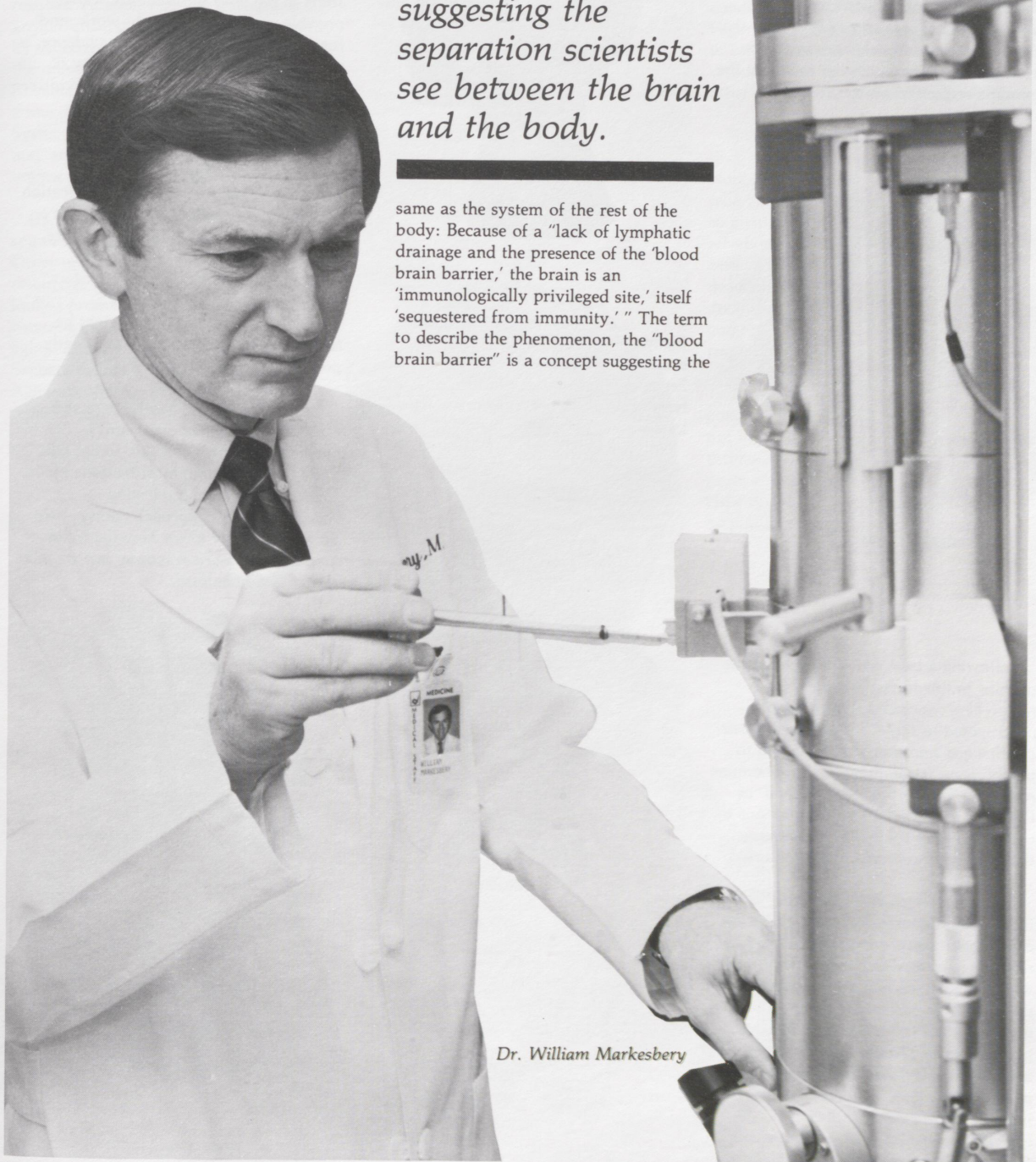
Roszman found Brooks' proposal intriguing. "I was interested in the unique site of the tumor," he said. "Brain tumors are peculiar. They rarely metastasize." The brain's circulatory system is not the

Dr. William Brooks



The term to describe the phenomenon, the "blood brain barrier" is a concept suggesting the separation scientists see between the brain and the body.

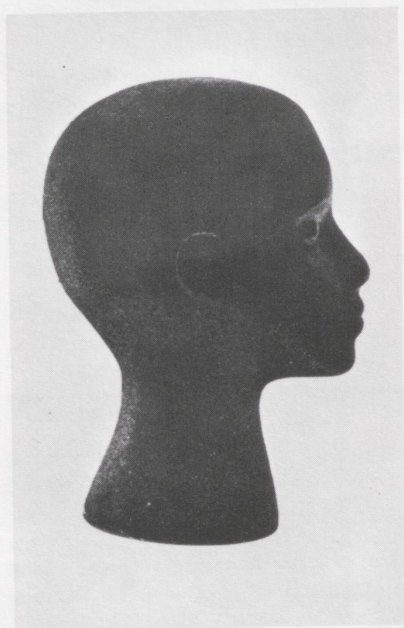
same as the system of the rest of the body: Because of a "lack of lymphatic drainage and the presence of the 'blood brain barrier,' the brain is an 'immunologically privileged site,' itself 'sequestered from immunity.'" The term to describe the phenomenon, the "blood brain barrier" is a concept suggesting the



Dr. William Markesbery

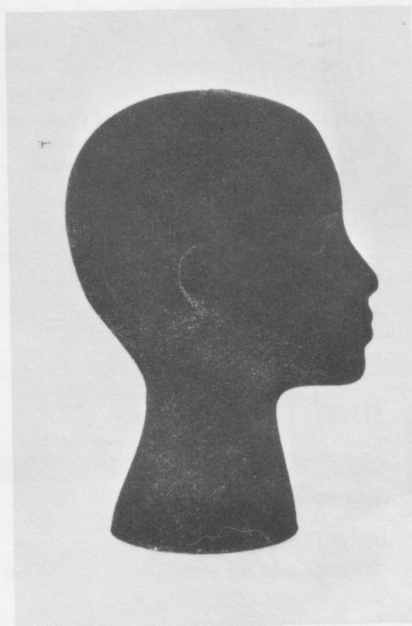
separation scientists see between the brain and the body.

But if the brain could be regarded as a separate entity, why should the general immunological response of brain tumor patients decline? "Often at the outset the patient is in pretty good general health," Roszman said. "But as the cancer grows the immune response weakens." One unconventional idea to explain this is that the tumor is causing changes in certain areas of the brain which can influence the immune response.

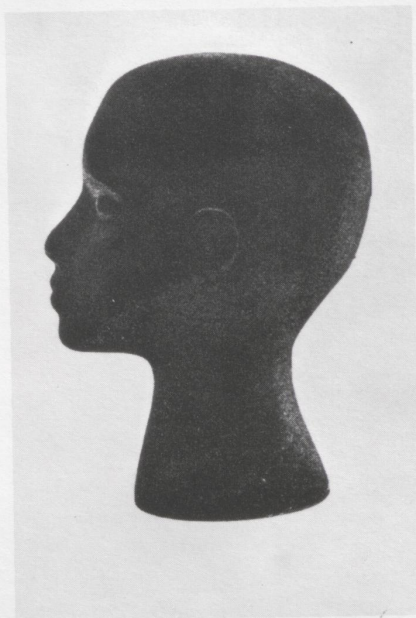


Following a long series of experiments on rats' brains to test this idea, the researchers concluded that the brain participated in some "modulation" (their conclusions were not strong enough to justify using "regulations") of the immune response. Simply put, they learned, as Roszman said, that "if you put lesions in certain areas of the brain you observe that immune reaction has been affected."

The research involved the study of cells involved in immune response. These are called macrophages and lymphocytes. By removing spleen tissue from an animal with lesions in certain areas of the brain the researcher can isolate these cells. One way of testing the spleen cells immune potential is by placing the cells in a tube along with substances which induce their proliferation; later a radioactive probe is inserted to provide the labeling of lymphocytes which are undergoing cell division. Then a comparison is made with



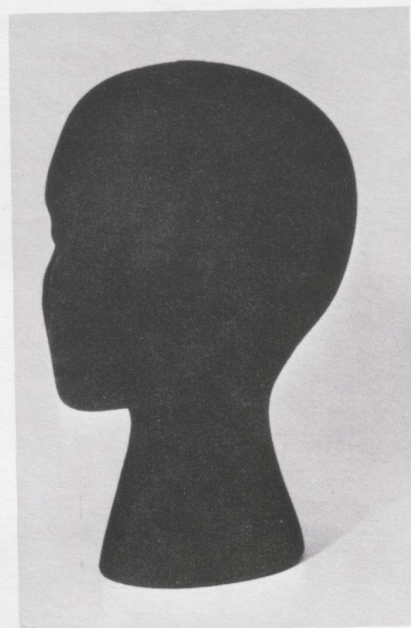
the lymphocytes of an animal whose brain has not been damaged with lesions. Fewer divisions of immunity producing lymphocytes are observed in animals with lesions.



Research has indicated the crucial role of the pituitary gland. Different results were obtained by placing identically located lesions in the brains of laboratory animals with and without intact pituitaries. The research suggested, Roszman said, that "the pituitary produced hormones which were in some way impinging on white cells and causing shifts in the level of immunity." One possible way that this might work, and for which the group has some evidence, is that hormones regulate the activity of macrophages which in turn has a positive or negative effect on the ability of lymphocytes to proliferate.

The problem, Roszman said, is determining the nature of communication between "two black boxes"—one, the brain, the other, the immune response. Both systems, he observed, "made extensive use of soluble signals for communication, so it was not unreasonable to think there might be cross talk. In fact, the evidence clearly points in that direction."

Roszman, Brooks, Markesbery and their associates have overheard a muttering undertone of this "cross talk," but a lot of research must be done before some of their more interesting speculations will approach reality. "We do not definitely know how the brain modulates immune response, but we have clues," Roszman said.



One of the next steps is to learn more about how hormones influence macrophages and lymphocytes. If the research is productive, scientists may begin to consider more seriously the ways that immunity might be adjusted to fight against disease—including cancer, which like other diseases, is identified by the immune system's scanning ability, and resisted. Another possible outcome is greater understanding of diseases caused by excessive or uncontrolled activity of the immune response itself: For example, Rheumatoid arthritis; Myasthenia Gravis, a muscle weakening disease; and Systemic Lupus Erythematosus, which may attack the heart, kidneys or other organs and may be fatal.

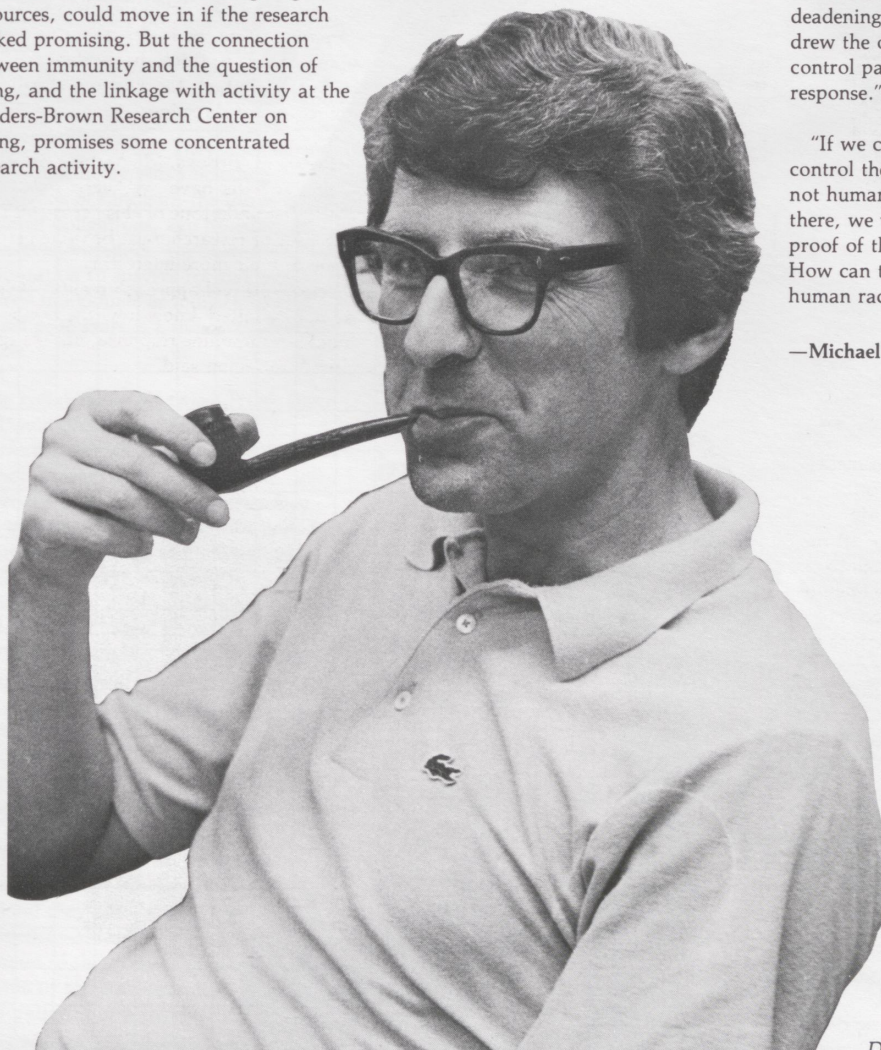
UK researchers hold a small and somewhat unsteady lead in this research. Other universities, commanding larger resources, could move in if the research looked promising. But the connection between immunity and the question of aging, and the linkage with activity at the Sanders-Brown Research Center on Aging, promises some concentrated research activity.

There are no clear indications how much research remains before investigators will understand the connections between the brain and the immune response. They want to continue their work with rats, employing more exactly placed and more extensive lesions and initiate studies to monitor the immune response in behaviorally conditioned rats. They have not yet begun to examine the possibility, implied in other research, that the immune response may be controlled by one or the other hemisphere of the brain.

Earlier in their research, Roszman and Brooks had conversations with Dr. Norman Shealy, the Wisconsin physician who has used biofeedback and autogenics to instruct people how to control pain, which previously had been beyond control except through the use of deadening drugs. From Shealy, Brooks drew the obvious inference: "If you can control pain, why not control immune response."

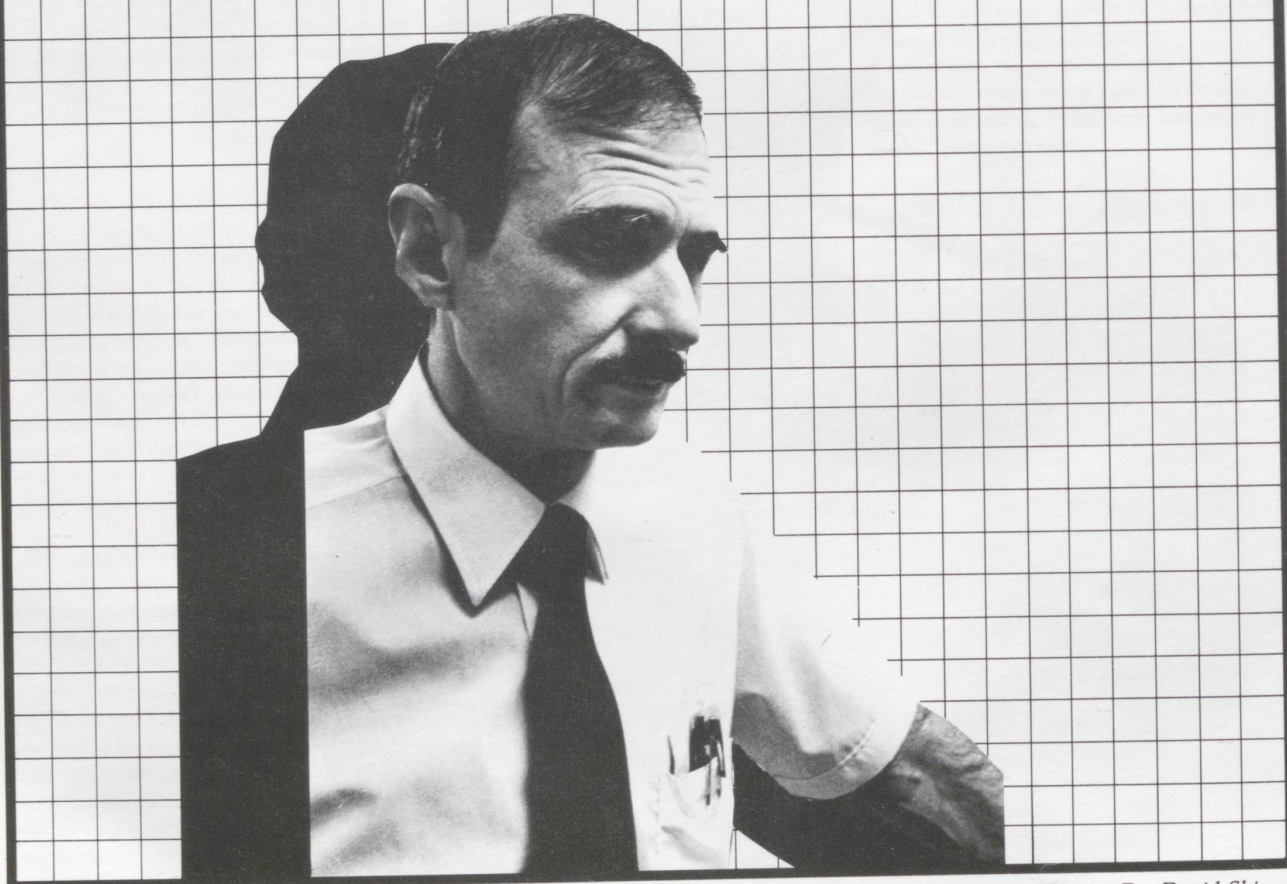
"If we can learn to condition animals to control the immune response, then why not humans?" Brooks asks. "If we succeed there, we will have met the ultimate proof of the value of medical research: How can the discovery be used by the human race to better itself."

—Michael J. Kirkhorn



Dr. Thomas Roszman

Dr. Frank Rizzo



Dr. David Shippy

COLLABORATION AT THE BOUNDARY

"We have had disagreements, and each of us has been proven wrong in front of the other, but we always come out with our dignity intact."

Professor Frank Rizzo speaking of his collaboration with Professor David Shippy

Enduring collaborations between researchers are rarer than enduring marriages or enduring business partnerships. They proceed from the early recognition of common interests and require the unselfish exchange of ideas and techniques, sensitivity, fairness, good humor, a lot of understanding and, most of all, mutual respect. They must survive all sorts of fluctuations (including fluctuations of funding), the intrusion of unrelated obligations, ego bruising, at times, even boredom. For such a collaboration to survive for five years between individuals as independent as tenured professors is a minor academic miracle.

The collaboration between Frank Rizzo and David Shippy, professors of engineering mechanics, is one of the more successful meetings of minds at the University of Kentucky. Together they have made fundamental contributions to an important method of analysis used worldwide to solve problems in engineering and applied science. Called the Boundary Integral Equation Method (BIE) or the Boundary Element Method, it allows for the swift analysis of issues as diverse as the finding of peak temperatures in diesel engine pistons, the measuring of the flow of water in an underground aquifer, or of the effect of a distant earthquake on a building.

Collaborations do not bring together unformed minds. When they are successful they unite—often by lucky coincidence—researchers already engaged in courses of inquiry which would have led some to some achievement without collaboration, but were enhanced by it. In this case the collaboration drew together

Shippy's newfound fascination with computer programming and the research which enabled Rizzo, in his Ph.D. dissertation in 1967, to offer the first demonstration that the method, which would later be called the BIE, could viably be applied to the study of elasticity, which is one of the crucial areas in which it is employed.

The collaboration began this way:

Rizzo: "I was somewhat analytically inclined as a student. I was interested in the methods of solution rather than the solution of particular problems.

"My professor was Marvin Stippes, one of the more prominent theorists in classical elasticity. He was a real scholar, concerned about the origins of ideas, how

A complicated three-dimensional elastic solid can be approximated by a bunch of little blocks joined together—like a mosaic. Each block is assumed to change its shape under pressure from its neighbors. The computer can keep track of the deformations of the little blocks and the forces between them.

the guys who made the fundamental contributions did it, whether and how they communicated with each other. He wanted us to go back and look at where things came from and to understand how key variables were related to other key variables.

"I wanted to do a thesis where there would be some contribution to methodology in the theory of elasticity. Stippes was crucial. The graduate students (at the University of Illinois, Champaign-Urbana) called him 'the master.' He was a true academic father figure. People admired him for his elegance and mastery of classical mathematics and his understanding of the world of applied science.

"In the course of a conversation about my thesis topic, Stippes asked me to look at a number of papers in an area analogous to but simpler than the theory of elasticity.

"These papers were written by a British scientist named Maurice Jaswon [later the chairman of Rizzo and Shippy's department at UK]. Then Stippes went on sabbatical. While he was gone my research took an unexpected turn which led to the writing of my Ph.D. dissertation in 1967.

"Jaswon was interested because I had extended some of his ideas to the more complicated theory of elasticity. My ignorance of certain relevant matters was lucky because it prevented me from making some of the mistakes which had plagued Jaswon even in the simpler theory.

"No one had any idea that 15 years down the road something called the BIE method would exist. When you do some pioneering work that later becomes interesting, people assume that you foresaw it all. You're accused of having all kinds of ideas early on that you never really had.

"Elasticity, simply described, is something like this: An object squeezed or deformed will assume its original size and shape when the squeezing forces are removed. You may know in advance the distribution of forces exerted on the surface, but you won't know the surface displacement until you actually solve the problem. The question I asked was, can I find the surface displacement from a knowledge of the surface force distribution without solving the whole problem first? The answer was yes."

After receiving his Ph.D. in 1963, Shippy participated in a National Science Foundation summer research program at Stanford University. He was eager to work in Palo Alto with Professor T.R. Kane, an authority on dynamics and vibrations—Shippy's specialty at the time.

Shippy: "At Stanford I got my first exposure to computers and I just fell in love with computer programming. By the end of the second summer, I was pretty adept at programming. By that time I was a member of the faculty at UK."

One day Frank Rizzo came to me and said he was wondering whether I was interested in collaboration. He said it would involve some unusual computing and that attracted me right away. I thought the project was interesting and potentially fruitful. I decided to be open minded. We had not even the vaguest idea where all this might lead. Eventually I started writing computer programs and one thing led to another."

The collaboration began in 1967. As is the case with so many research projects, the computer was the indispensable third party; without its existence there would have been no BIE and no collaboration.

"It was always possible to write down equations describing some problem," Rizzo said. "You could solve these equations for simple geometrics and simple material behavior. But when you had a real situation you had to go to experimentation or you had to make an unrealistically ideal facsimile of the problem just to obtain ballpark figures. The computer changed all that. It allows you to keep the realism in the problem and solve the equations which describe what you're interested in with very small error. Dave's big love is to expect answers to complicated problems and see them come out of the computer."

Almost everyone doing engineering analysis uses the computer. What is special about the BIE method? "You know how any curve such as a sine wave or a circle can be approximated by straight line segments joined together," Shippy explains. "And if the line segments are numerous enough, the approximation will be very good indeed. In a similar way, a complicated three-dimensional elastic solid can be approximated by a bunch of little blocks joined together—like a mosaic. Each block is assumed to change its shape under pressure from its neighbors. The computer can keep track of the deformations of the little blocks and the forces between them, and give this information to the analyst."

"This is great, but very predictable. You expect to be able to use the computer this way and you can, very effectively, although sometimes handling the amount of data necessary for accuracy can be expensive and tedious."

"The BIE approach is a bit different then this. It takes a major analytical step before the computer is ever approached."

The mathematical breakthrough which earned Rizzo and Shippy their international reputations was this: They moved from analyses of the imaginary little "blocks" used to simulate problems to analysis of only the surface, or boundary, of the bodies.

"We just cut up the surface of the body It's a little like painting a gridwork on the surface and making our analysis from that. The implications of that for computational analysis are just enormous."

"The very formulation of the problem is changed at the outset," Rizzo explained. "The problem is converted to one involving integral equations rather than differential ones. Thus the dimension of the problem is reduced by one, so the desired information throughout the body, formerly obtained through the 'little blocks,' is now obtainable through little area elements on the surface of boundary of the body only. An engineer using the BIE method could learn most of what he needed to know about temperature in the diesel piston by making a computer analysis of its surface. This feature of the BIE has obvious implications in convenience—the amount of data to be handled, if nothing else. But there are other advantages in accuracy, economy and efficiency."

"We just cut up the surface of the body," Shippy said. "It's a little like painting a gridwork on the surface and making our analysis from that. The implications of that for computational analysis are just enormous."

The National Science Foundation and the Air Force, which have provided support for this research, apparently agree with Shippy's assessment.

The two-fold nature of the careers of Rizzo and Shippy is unusual in a university, which encourages individual achievement, but they have detected no serious impediments. They recognize how closely bound together they are.

"We spend a lot of time communicating with people, helping to arrange conferences, reviewing papers and proposals," Rizzo said. "We really have got a lot of connections tied to both of us. Sometimes we proceed independently on an aspect of a project. Then we feel the need to get together, again. Most of our research is devoted to a mutual endeavor. There is no reason to think other than that it will continue. We complement each other's work, and each of us does what he does best and what he likes to do."

"Initially, I was the theorist who had hoped to collaborate with Shippy because I'd heard that he had a relationship with the computer like a conductor has with his orchestra. This turned out to be true, but Dave is an excellent theorist, as well as a computer virtuoso. The collaboration for all these years has depended heavily on that fact."

"Frank shies away from programming," Shippy said. "But he has a good understanding of what the computer does in each part of our complicated programs. This has been important too."

A researcher who is lucky will make one important contribution to his field of research, quite often in youth or early middle age, then spend the remainder of his or her career elaborating, adapting, calculating the implications, applying, teaching. Rizzo and Shippy acknowledge that their contribution to the BIE method may be both keystone and capstone to their careers. They have experienced the satisfaction, which nourishes the creative intellect, of drawing together notions and ideas into a body of work both valuable and well received.

—Michael Kirkhorn

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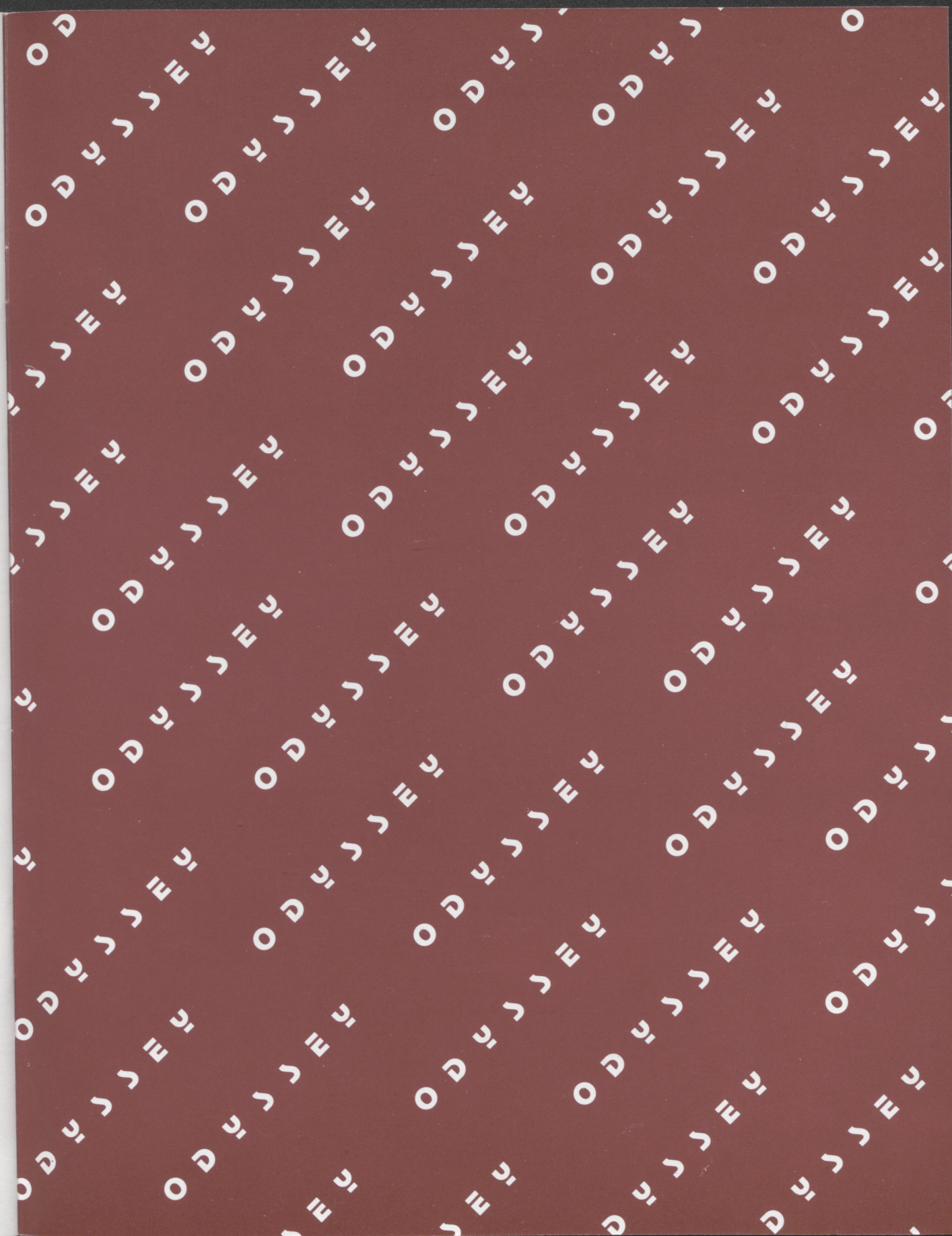
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