

ODYSSEY

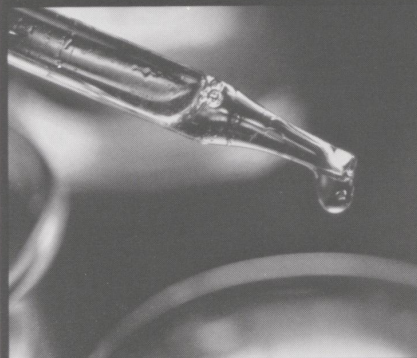
SUMMER · A MAGAZINE OF UNIVERSITY OF KENTUCKY RESEARCH · 1987



MAGIC BULLETS FOR VIRUSES: DISCOVERING THE SECRETS OF VSV

ODYSSEY

SUMMER • A MAGAZINE OF UNIVERSITY OF KENTUCKY RESEARCH • 1987



MAGIC BULLETS FOR VIRUSES-DISCOVERING THE SECRETS OF VSV

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 edu-

cation 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 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.

copy 1

University Archives
Margaret I. King Library - North
University of Kentucky
Lexington, Kentucky 40506

Volume V, No. 2

ODYSSEY is a magazine published by the University of Kentucky Research Foundation under the auspices of the Vice Chancellor for Research and the Dean of the Graduate School. Each issue of ODYSSEY describes only a few of the many University of Kentucky research projects underway in a variety of areas.

Requests for permission to reprint material and readers comments regarding ODYSSEY are welcome and should be sent to the Editor, University of Kentucky Research Foundation, University of Kentucky (0057), Lexington, Kentucky 40506, Phone 606-257-8297.

The publication of ODYSSEY is not financed by state-appropriated funds.

Editor: Susan H. Donohew

Designer: Shear & Shear

Publications Assistant: Sharon J. Turner

Contributing Writers: Lissa Atkins, Maria Braden, Pam Fahey, Markel Tumlin, Jeff Worley

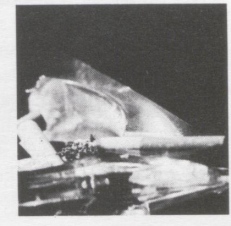
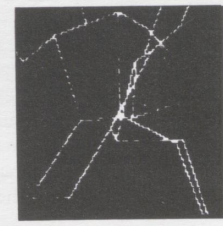
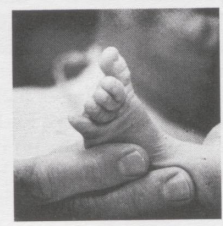
Printing: UK Printing Services

Credits: photos on pp. 3, 6, 10, 25, 29, 31, 33 by Alen J. Malott; photos on pp. 9, 14-21, 26, 32, 34, 36 by Ken Goad; cover photo by Comstock. Illustrations on pp. 23, 24 by Topps Chewing Gum, Inc.; illustration on pg. 27 by Shear & Shear.

CONTENTS



Magic Bullets for Viruses: Discovering the Secrets of VSV	page 2
Superpower Semantics	7
A Revolutionary in Aerosol Science	10
Helping Newborns to Breathe	14
Pitcher Science	22
Who Makes the Choices for the Elderly?	25
Smokeless Tobacco: An Unsafe Alternative	27
Smoking and the Immune Response	31
Helping to Break the Habit	33
Walking Tall	35



Received in Campus mail, June 1987

MAGIC BULLETS FOR VIRUSES: DISCOVERING THE SECRETS OF VSV



by Jeff Worley

The saboteurs rush the wall and are through in almost no time. Encountering little resistance, they work their way toward their objective—the “big machine”—and capture it. Stage one of the subversion is completed.

The story line may sound familiar, reminiscent perhaps of the commando raid in *The Guns of Navarone*. The “actors” in this scenario, however, are viruses—tiny blueprints encased in a protective “coat.” Dr. Judith Lesnaw and her associates, Dr. David Hammond and pre-doctoral student Andy Feldhaus, hope to rewrite the script so that in the future these saboteurs find themselves on Mission Impossible.

Viruses are small, so small that they can be seen only through an electron microscope. The simplest viruses consist merely of nucleic acids, pieces of genetic information which can be either DNA or RNA, wrapped in a protein package. Unlike cells, viruses contain no machines for protein syn-

thesis; viruses cannot, by themselves, make the energy or building blocks needed to sustain their existence. Unique parasites, viruses exist on the threshold of life, totally dependent on the host cell for replication.

The process by which a virus replicates is a fascinating one. To compensate for its deficiencies, the virus must take over the cellular machinery and subvert it to its own use. The virus does so by first attaching itself to specific sites on the cell's surface, where it is enveloped by the cell membrane and drawn inside. Once inside, the virus removes its protein coat, and the viral blueprints instruct the cell to make two kinds of proteins: structural proteins that form new viral coats and a viral enzyme, the replicase, which makes new blueprints.

Newly assembled viruses then begin to make their escape from the cell. Some types burst dramatically through the cell wall; others bud out of the cell more gently. Hundreds, or

An electron microscope produced this greatly magnified photograph which shows the virion with the “lid” popped off. Note the little dotted line trail which is the genetic information spilling out of the virion. This photograph, along with the other magnified photographs in this article, was taken in 1973. With the new electron microscope planned for the Markey Cancer Center as part of the Core Facilities, the capability for producing these types of photographs will be infinitely improved.

thousands, of new viruses begin the life cycle again in a new cell.

“We want to find out exactly **how** the virus multiplies within the cell—what part of the cell it borrows. We also want to understand how the virus damages the living cell,” Lesnaw says. “The virus, though small, cleverly changes the cell's machinery. The altered machinery now responds to the viruses' instructions, not those of the host.”

To underscore the relative difficulty of combatting viral infection, Lesnaw contrasts it with bacterial infection. Bacteria, like the hosts they infect, are cells; but the bacterial machinery differs from the host cell's machinery. Bacterial infection can be combatted with antibiotics that inactivate the bacterias but not the host machines.

"The virus, however, uses the cell's materials and machinery. We cannot destroy the machines that make these viral particles because the machines are us. This kind of cure would kill the patient," Lesnaw explained. Instead, virologists seek to identify a crucial part of the virus that makes it different from the host.

Lesnaw's research is focused on the study of the vesicular stomatitis virus (VSV), first isolated from small lesions on the tongues of cattle. VSV is a negative-strand virus, a category which includes rabies, influenza, measles, and mumps. It serves as an excellent model system for studying this group of viruses because it's very similar to the deadly viruses, yet is not itself a deadly human pathogen. Moreover, it's easy to grow in tissue culture and easy to purify. Lesnaw has been probing the secrets of VSV since 1970.

In her research, Lesnaw studies how the negative-strand VSV uses the host cell to reproduce itself. When in its latent state as a virion—a metabolically inert particle composed of an inner core of nucleic acid and protein, and a bullet-shaped membrane of protein and fat—VSV encounters a host cell, the outer membrane of the virion is stripped off and the inner core enters the cell.

Now the virus runs into a problem: host cells are unable to copy RNA into RNA. The virus solves this dilemma by bringing into the cell its own enzymes to copy the necessary genetic information into mRNA. This new strand then directs the host cell's ribosomes to make new viral proteins, some of which produce new inner cores and others of which produce new outer membranes. The cores and membranes then assemble

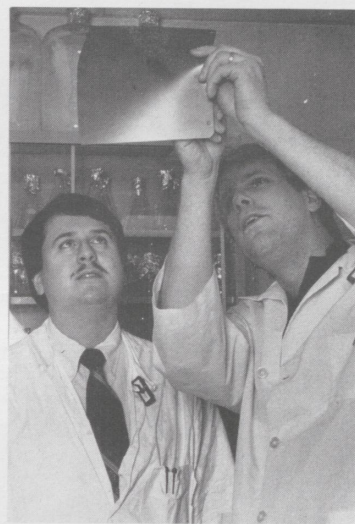
and these new virions bud out of the cell, ready to infect other cells.

To understand how the virus replicates, Lesnaw is attempting to discover some property of the virus that differs from its host. "A likely target is the viral enzymes used to make the viral nucleic acid, the replicases and transcriptases that make the messenger RNA," Lesnaw says. "If we can understand these enzymes, we can design a 'magic bullet,' a drug that will be able to distinguish between viral material and cellular material."

Lesnaw and her research team are now focusing their attention on VSV's largest enzyme, the L protein. This enzyme catalyzes six chemical reactions, each of which might be carried out by a separate enzyme in a different virus-host cell system. "This enzyme is unique to the virus," Lesnaw explained, "so if we can find the active regions on the molecule—for example, areas where the binding of building blocks takes place or regions that interact with the original blueprint that's being copied—then we can develop magic bullets that will go to these specific regions and inactivate them. If we can block the viruses' replication process, we'll have a cure for the infection." The information gleaned from the VSV studies will suggest strategies for prevention and treatment of other negative-strand viruses.

The researchers are pursuing two related approaches to solve the mysteries of the L protein. One involves the analysis of VSV mutants whose genetic information has been altered in such a way that the L protein it specifies can no longer carry out all its normal functions. This approach is part of the dissertation research of doctoral student Andrew Feldhaus. He is using techniques called nucleotide sequencing to identify the sequences of bases on the viral RNA that specify the structure of the viral proteins. His goal is to find the active sites in the L protein by mapping the location of functional mutations.

"Mutants help us out," Feldhaus



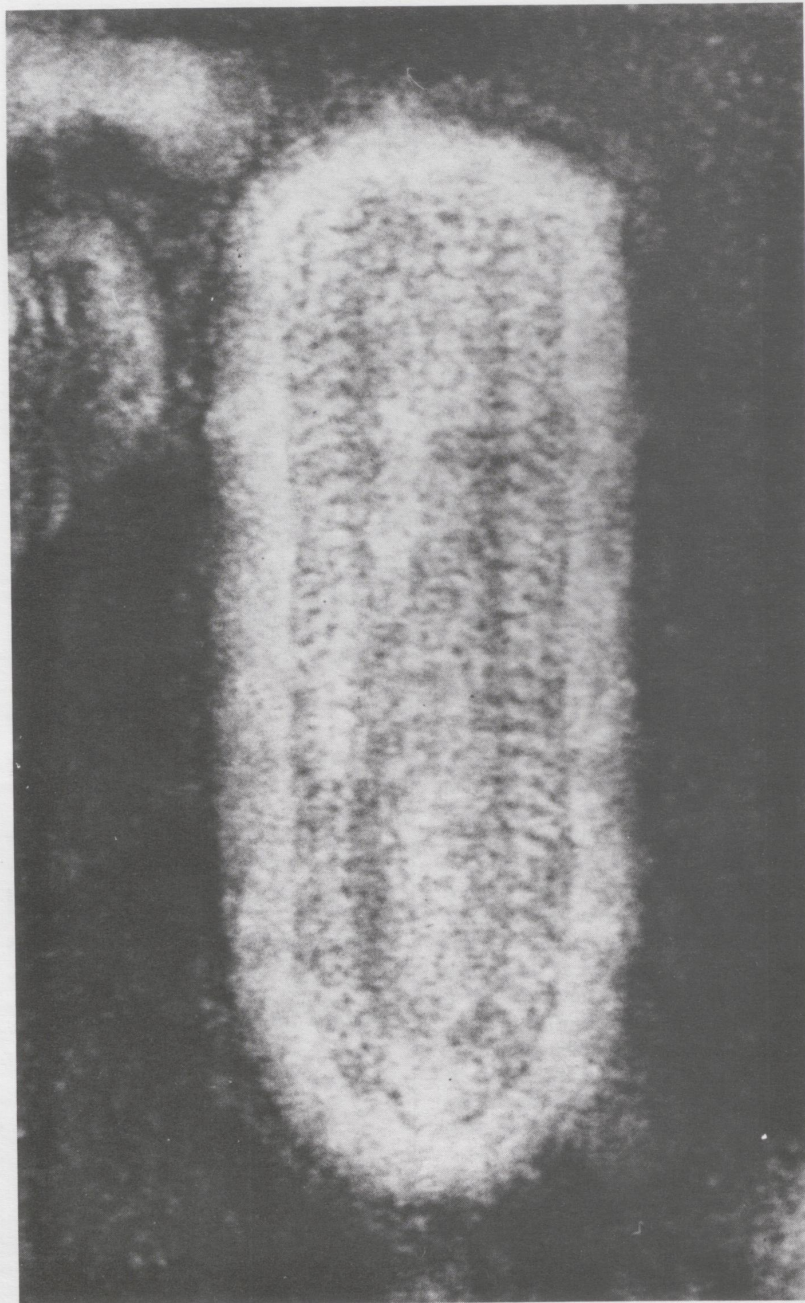
Examining a film of sequencing gel are Dr. David Hammond, left, native of Midland, Michigan, and pre-doctoral student Andrew Feldhaus, from Covington, Kentucky.

"We cannot destroy the machines that make these viral particles because the machines are us. This kind of cure would kill the patient."

continued on page 4

MAGIC BULLETS FOR VIRUSES:
DISCOVER THE SECRETS OF VSV

"If we can block the viruses' replication process, we'll have a cure for the infection."



This is a pure virus particle. Shaped like a bullet with whiskers, it's Greek name is "Rhabdovirus."

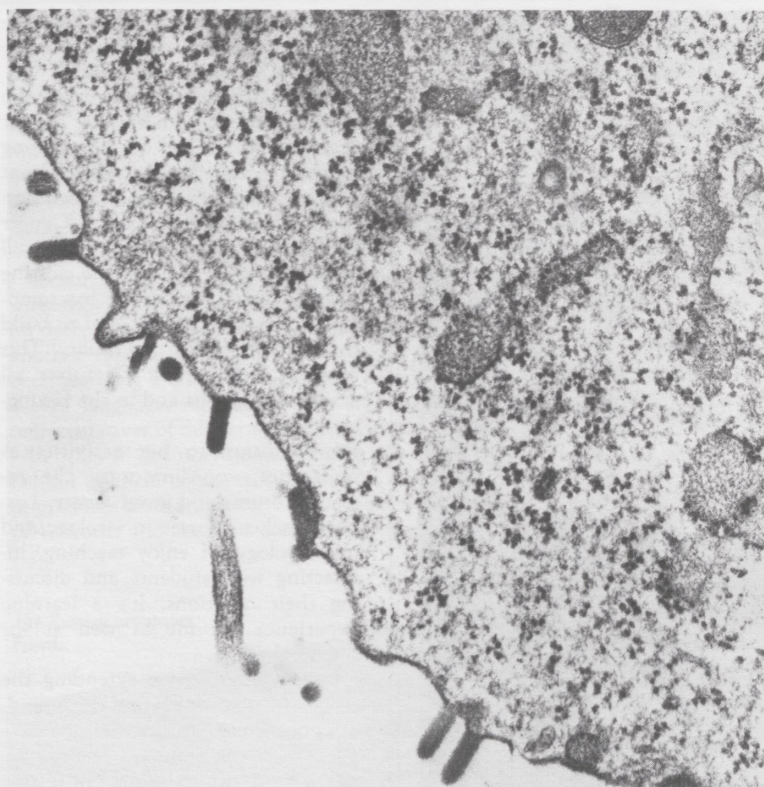
explains. "Once we discover in what ways a molecule is deficient, we can begin to determine how this deficiency alters the function of the three-dimensional structure of the protein."

A second approach exploits the technological innovation of light-activated radioactive probes. One of the originators of this technique is Dr. Boyd Haley, who is now a member of the UK faculty in the Lucille Parker Markey Cancer Center. This approach is being used by post-doctoral fellow Dr. David Hammond. "We know that enzymes carry out specific functions—they interact and bind," Hammond explained. "To attempt to determine which enzymes are involved in virus reproduction, we have designed a radioactive molecule that is structurally specific, similar to the substrate, but altered so that it binds tightly."

The light-activated radioactive probe, then, is a normal enzyme substrate into which both an atom of radioactivity and a highly unstable azide bond have been incorporated. In the presence of the enzyme, the probe can bind to the enzyme's active site. If, when it's bound, the probe is exposed to certain frequencies of light, the azide bond breaks and forms an irreversible bond between the enzyme and the probe.

The enzyme can then be cut into small fragments, called peptides, which can be separated on the basis of size and charge. The peptide to which the probe is attached can be identified by the decay of the radioactivity incorporated into the probe. Using these probes, then, Hammond hopes to identify the active sites in the L protein. The analysis of peptides is carried out in the Markey Cancer Center Macromolecular Structure Facility.

"Hopefully, we'll find that one of these areas, when 'shot,' will no longer be active in the replication process," Hammond says. "We'll be able to make magic bullets to neutralize this action."



These are examples of the virus, the black bullet-shaped objects at the edge of the cell wall, budding from a cell membrane—the final step in the virus assembly process. There

are one million cells in one square inch of human skin and approximately 500 of these viruses could fit into one cell.

Lesnaw points out that another major benefit of viral research is the discovery of how cellular machines work and the ways in which multifunctional proteins carry out their assigned tasks. "Viruses, in this view, are not altogether nasty. We are using the virus itself as a probe to examine normal cellular functions: the virus becomes a window to the cell."

Although Lesnaw devotes much of her time and energy to the study of viruses, she also enjoys interaction with students—she teaches courses in virology and microbiology—and with investigators from other disciplines. "I was attracted to UK initially," she says, "because there is such a wide variety of activity at one campus—the

College of Arts and Sciences, a fine medical center, and the Lucille Parker Markey Cancer Center. Here, I can carry on a research program and be involved in teaching at the same time." She also gives lectures in community programs, such as UK's Saturday Seminar Series which brings "science to the public."

With a generous grant from the National Institute of Health, the research team will continue to probe the secrets of VSV. Lesnaw emphasizes the point that their research may have far-reaching significance: "Many of the most important biological breakthroughs, our understanding of life itself, has come from the study of viruses."

JUDITH LESNAW: MICROBE HUNTER

As a sixth-grader Judith Lesnaw thought that she had already read every science fiction book in the school library. Then she found one, obviously mis-shelved, that she hadn't read: **Microbe Hunters**. The book may have changed her life.

Microbe Hunters, it turned out, was not science fiction, but science fact—the story of the history of microbiology. "Actually, the story is somewhat in the vein of science fiction, the actions of small creatures you can't see causing devastating effects on the human population. I was entirely captivated by the idea of a life form so small and simple, by the concept of an entire universe in a drop of water," Lesnaw says.

Her interest in the study of viruses led her to the University of Illinois, where Lesnaw completed an undergraduate degree in microbiology and graduate degrees in botany and biology. In graduate school she took a class from the well-known virologist Sol Spiegelman, and under the direction of Eli Reichmann focused her research on the tobacco necrosis virus and its satellite, a relatively small and simple plant system.

By 1971, her primary interest had shifted to the study of the animal virus vesicular stomatitis virus, or

continued on page 6

"The virus, though small, cleverly changes the cell's machinery. The altered machinery now responds to the viruses' instructions, not those of the host."

-Judith Lesnaw



VSV. "In preparation for my studies of VSV, I spent one month in the laboratory of Dr. Craig Pringle at the Institute of Virology in Glasgow, Scotland. Armed with a battery of new techniques learned from Dr. Pringle, I returned to Eli Reichmann's laboratory," Lesnaw explains. Three years later, she came to UK and set up an independent laboratory to continue her studies of VSV.

In her 13 years at UK, Lesnaw has seen significant changes. "First of all, there has been a tremendous increase in the number of basic scientists hired

in molecular cell biology. There has also been a definite movement toward interdisciplinary collaboration—this is a wonderful thing. My collaborations with the departments of Biochemistry and Plant Pathology have continued to develop."

One indication of this movement toward interdisciplinary study is the molecular cell biology weekly research forum. Lesnaw is the program coordinator for this group. "Fifty to 60 people—professors, graduate students, and post-doctoral fellows—meet every week to exchange ideas and discuss problems with research projects.

We also update each other concerning new technological breakthroughs," Lesnaw says.

Many of the scientists in this group will also benefit from another project that Lesnaw worked on—the writing of the recently funded Core Grant which brought national recognition to the Lucille Parker Markey Cancer Center. She says that these funds will help to support some of the existing Core facilities, such as the macromolecular structure facility, and to build the electron microscope facility. This funding will benefit scientists all across the campus and in the Lexington region.

In addition to her activities as researcher, coordinator of the research forum, and grant writer, Lesnaw teaches courses in virology and microbiology. "I enjoy teaching, interacting with students and discussing their questions. It's a learning experience for me as well as for them," she says.

Lesnaw also enjoys extending the scope of her work beyond the boundaries of the campus. Last fall she gave a lecture in the Saturday Seminar Series, a forum which allows UK faculty to present and discuss their ideas with the general public. "I believe that it's exciting and important to bring science to the public."

What Lesnaw brings to science is a fiery enthusiasm. "I like working with Judy because she adds a lot of excitement and enthusiasm to our work. It's easy to get caught up in that," says Andrew Feldhaus, a doctoral candidate who works with researcher David Hammond and Lesnaw in their study of VSV.

Lesnaw is excited about the challenges virologists face as the 21st century grows nearer. "There's so much that needs to be done. My hope is that by the year 2000 we will have learned a great deal about how model systems such as VSV function so that we can translate the strategies we've devised into ways of looking at more complex systems." —Jeff Worley

SUPERPOWER SEMANTICS

by Jeff Worley

Hanging conspicuously on a wall of Political Science Professor Daniel Nelson's office 16 floors above the University of Kentucky campus is an M.C. Escher print. As usual, Escher is playing tricks on us: pillars connect floors to ceilings at impossible angles; a winding staircase seems to rise perceptibly step by step, but when we look again we see that it is taking the two climbers no higher at all.

Escher makes the point that things are not what they appear to be at first glance. His artful deception is, in a sense, a visual analogy to another type of duplicity which Nelson has been studying for several years—the deceptive use of language, especially when utilized by representatives of different political systems.

In order to document differences in meaning behind political concepts, Nelson and a team of graduate assistants have researched the use of 40 words and concepts common in interna-

tional discourse. The study is focused on political language as used by authoritative speakers in the United States and the Soviet Union.

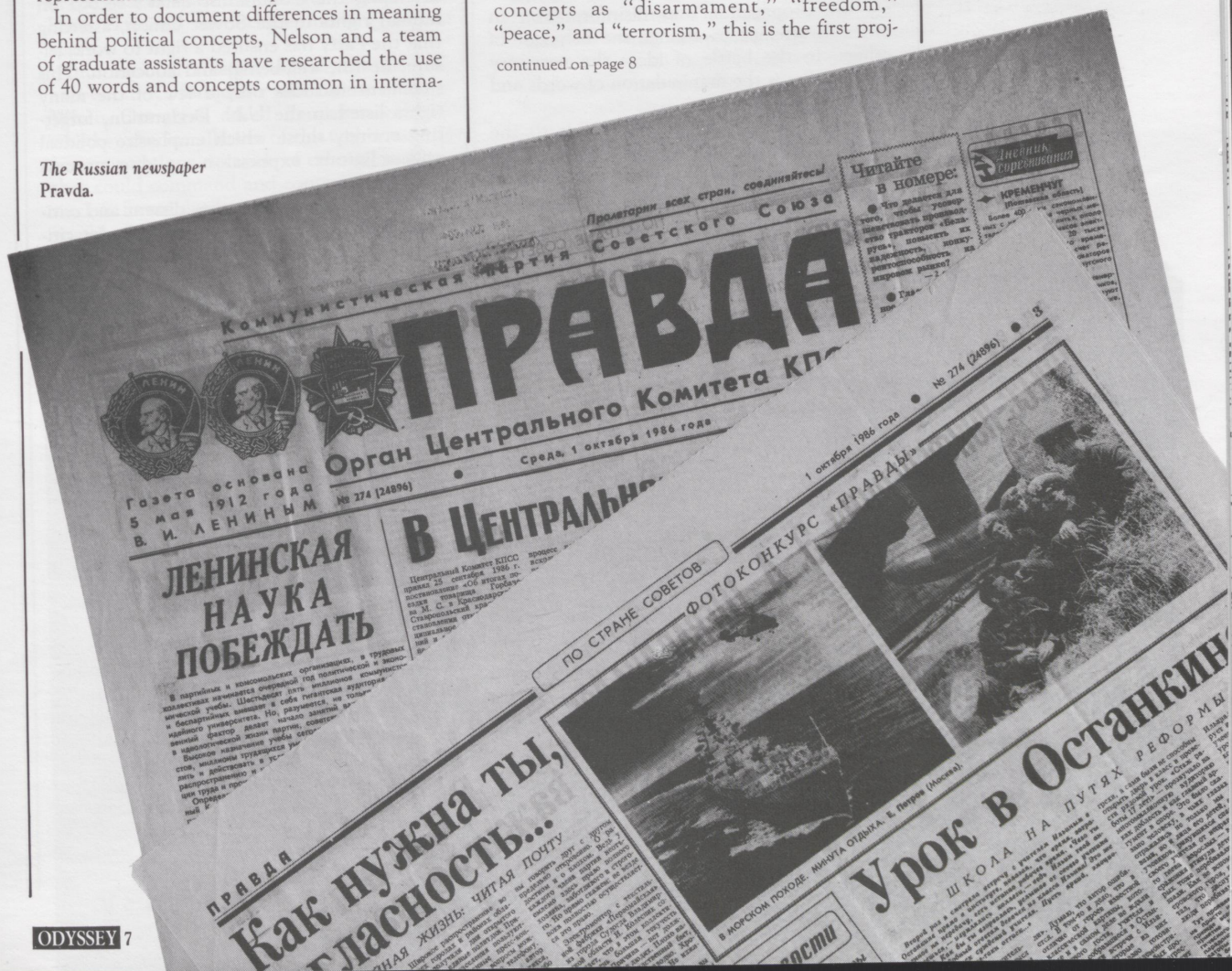
"To insure accuracy, we have utilized only original sources—quotes by Soviet and American leaders from established publications. We have purposely varied our citations from any one source, *Pravda* or *Izvestia*, for example, or any one spokesman," Nelson says. "This is an academic project which is generating even-handed essays that state succinctly what U.S. and Soviet usages are."

Nelson stresses the point that the purpose is not to create any anti-Soviet statement; the objective is to provide useful information.

Although there are dictionaries and other reference tools that deal with such political concepts as "disarmament," "freedom," "peace," and "terrorism," this is the first proj-

continued on page 8

The Russian newspaper
Pravda.



"subversive activity." Such political and legal aspects of human rights are, however, often discussed by Soviet leaders or journalists when commenting on conditions within the U.S. For example, Soviet journalists seek to portray cases such as the arrest or conviction of black, American Indian, or other minorities as *de facto* "political repression."

Put simply, the U.S.S.R. expands or contracts the meaning of human rights as needed in an attempt to fortify its position.

Although not a part of the Nelson study, others maintain that similar language manipulation is evident in U.S. policies. For example, in a recent article investigative reporter Tim Weiner of *Knight Rider*, points out that the Pentagon's recently publicized interpretation of the "use of space for peaceful purposes" has been extended to include military uses of space.

International treaties, signed by the U.S. and U.S.S.R., forbid the military use of space. When Congress asked Pentagon officials whether the installation of the C3I systems (a communications network of orbiting satellites that could command and control the nation's nuclear forces during and after World War III) would violate these agreements, the Pentagon replied, Weiner reported, that the U.S. interprets "the right to use space for peaceful purposes to include military uses of space to promote peace in the world."

In his study of semantic corruption, Nelson has had his "worst fears confirmed." "In looking over great amounts of material, I believe that the two Superpowers are still very far apart in terms of speaking to each other; instead, they continue to talk past each other."

The problem, Nelson says, is not in the denotation, or dictionary meaning, of words, but in their connotations, the meanings suggested by or associated with the words. "Even when the denotation of a word is identical ('unemployment' is when people are out of work), the Superpowers accuse each other of failing to take into consideration the needs of the workers. And connotation can be manipulated for political purposes regardless of denotation."

Connotation especially breaks down when sides begin to cite examples. "Genocide." Where does it exist, under what conditions? When has it occurred? The U.S. and U.S.S.R. would agree about genocide during the Nazi period, but there is no agreement about other

instances in which thousands of people were systematically killed. In discussing Idi Amin's reign in Uganda, for example, the U.S. refers to the deaths of hundreds of thousands of Ugandans as genocide; the U.S.S.R. does not use the term to refer to these same deaths. The Soviets, on the other hand, characterize as genocidal those South African policies that have led to the killing of thousands of blacks; the Reagan Administration does not see it that way.

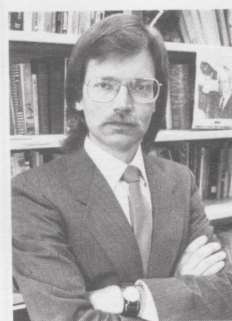
"The lack of agreement about meanings is sometimes quite purposeful. To acknowledge differences in meaning is to acknowledge that there are two valid interpretations," Nelson pointed out.

Problems of communication are not just a function of language use, but a function of entrenched mistrust. The conceptualization of language is merely symptomatic of underlying differences, and its use is modified according to the exigencies of events.

Nelson adds that the gulf of understanding widens when the Superpowers take hard-line positions, for example, the Soviet Union on Czechoslovakia in 1968 and Afghanistan in 1979, or when leaders take strong ideological stances. "Ronald Reagan's use of language in his 'Evil Empire' speech was clearly inflammatory. The choice of modifiers was not designed to calm nerves," Nelson said.

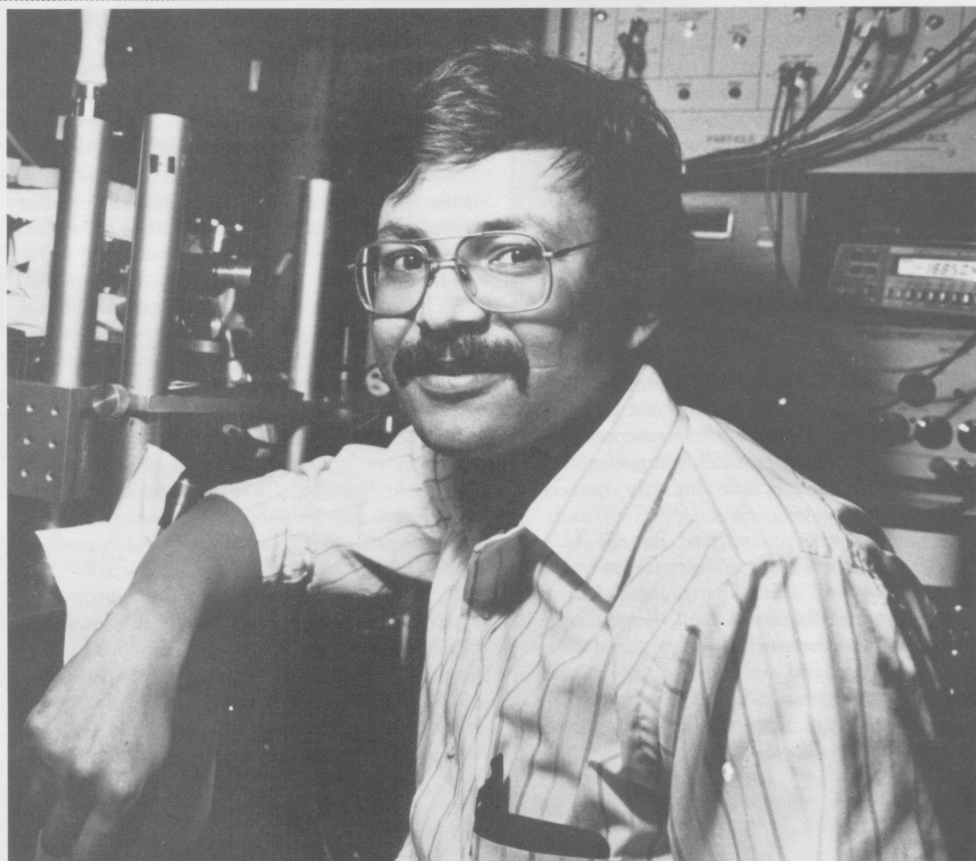
Although there might seem to be indications that the problem of communication is worsening, Nelson believes that this is not the case. "The capabilities to communicate are greater than they've ever been. Many universities around the U.S. are now receiving, on a daily basis, the Soviet's evening news program *Vremya* on satellite dish. The long-range prognosis is that the two sides will have a greater understanding of these terms they use in the political arena," Nelson commented.

He hopes that this project will lead to a stronger concordance between the Superpowers. Research has been completed on 35 of the 40 terms selected by the U.S. Information Agency, and 20 have been sent to diplomatic posts in booklet form. "Soon," Nelson says, "all 40 essays will be available in thousands of copies, handed out or mailed out all over the world."



Dan Nelson, Political Science

A REVOLUTIONARY IN AEROSOL SCIENCE



Asit Ray, Chemical Engineering

by Lissa D. Atkins

Dr. Asit Ray is a modern pioneer. His frontier is not the wide open range but the minute realm of molecular layers; his tools are not an ax and plow but an electrodynamic balance and laser. However, like the determined settlers who discovered new lands to inhabit, the chemical engineering professor has opened up a previously unknown area in the field of aerosol science.

Ray is studying aerosol systems, a name which, for most people, conjures images of spray cans. However, in Ray's research, aerosols are the suspension of small particles in air or gas. The particles are the intermediate stage in a vapor to liquid or vapor to solid transformation process. Typically between .01-25 microns in diameter (a human hair is approximately 25 microns), the particles cannot be seen with the naked eye. A cubic centimeter

(the equivalent of five teaspoons) may contain as many as 100 million particles.

Examples of the vapor to liquid and vapor to solid transformation processes are the formation of water and ice. As water vapor in clouds begins to cool, small nuclei or clusters of typically less than 100 molecules begin to form. These nuclei are thermodynamically unstable and may continue to grow or evaporate. If they do continue growing, the clusters reach an aerosol stage and are approximately several hundred molecular layers thick. With continued growth, the particles form liquid droplets which then may fall as rain, or at very cold temperatures, form solid ice. Aerosol systems are also found in air pollution and in the formation of cigarette smoke and paint pigments.

Ray's work in aerosol science began in 1975

when he was a graduate student at Clarkson University (formerly Clarkson College of Technology) in New York. Because of the lack of technology at that time, most aerosol studies were carried out by researchers who had to look at the entire cloud. Isolating one particle and watching it grow or evaporate couldn't be done. Ray and doctoral advisor E. J. Davis conquered these limitations by developing a combination electrodynamic balance and laser scattering device.

"This technology revolutionized the field of aerosol science," says Dr. Len Peters, UK associate dean for research. "Every major aerosol lab, industrial or academic, has one or is contemplating getting one. The number of published papers about experiments in which this device was used has doubled, maybe tripled, each year since Ray first introduced it."

With the electrodynamic balance, Ray isolates a particle by charging it and then placing it in an electrical field. The balance is housed inside a vacuum chamber which evacuates through a turbomolecular pump. The environment is precisely controlled: the temperature is maintained within 0.1 degrees C and the pressure is controlled with an accuracy of 1 part in 10,000. In this state, a particle can be stably suspended (without any vibrations) for several days. An improved version of an earlier droplet suspension technique, Ray's chamber prevents the horizontal drifting of a particle and allows him to precisely control its position. This ability is crucial for him to obtain accurate results with the second aspect of his device—the laser.

By modifying other scientists' ideas about the properties of scattered light, Ray uses the laser to "see" the submicron particle. After stably suspending the particle in the chamber, Ray strikes it with the laser beam; exact positioning of the particle in the chamber enables Ray to do this precisely. Some of the radiation is absorbed by the particle while the rest is scattered at different angles. By measuring the intensity of the radiation that is scattered as a function of angle, Ray determines the particle's shape and size; the index of refraction reveals its chemical composition. These different properties reflect the various behaviors of the particles. For example, in smog the particles' size determines how they will scatter light and thus affect atmospheric visibility. Since smog particles are constantly changing, it is important to understand how they behave at various sizes. With smoke particles, their size

determines where they will settle in the respiratory system. The chemical composition indicates how reactive and chemically toxic a particle is.

Since finishing his graduate work and coming to UK in 1980, Ray has continued to modify his techniques and begun to apply them to specific aerosol systems. His improvements include a better electrodynamic balance, increased scattered light resolution, and the stable suspension of a particle at pressures less than one billionth of atmosphere. With these improvements, Ray can study smaller particles, gather more accurate data, and examine the surface molecular layer of a particle, typically several hundred molecular layers thick, to determine if it is homogenous or of two distinct phases.

Since 1981, Ray has been concentrating on the study of smoke particles. In cigarettes, the combustion of tobacco generates vapor. When it starts to cool, such as in the humid air in the lungs, particles begin to form. They may continue to grow or evaporate. If the particles do grow, then depending upon their size, they will deposit in different regions of the respiratory system.

"So many things are happening in this one small smoke particle," says Ray. "It provides a really good picture of phenomena in aerosols. With my techniques, we can experimentally examine each phenomena in isolation from others. This has really not been done before because the techniques have not been there. In this area, the research used to be more empirical, but now we are looking at things from a fundamental point of view."

continued on page 12

One application of Ray's research may be learning how to remove undesirable components from cigarette smoke while increasing the desirable ones.

Besides the basic science—size, shape, chemical composition and mass of a smoke particle—Ray is studying fundamental processes associated with an aerosol system. These include the formation of particles, the transfer of material to and from the particle and vapor phases, and the particle's surface actions. He's also introducing various concentrations of reactive gases or vapor and watching their interaction with the particle.

A variety of industries would benefit from the understanding and improvement of these fundamental processes. For example, in the paint pigment industry, the particles must be of a certain size; accelerating their rate of growth would save time, manpower, and money. Furthermore, aerosols could be used to dramatically increase the efficiency of certain chemical reactions.

When Ray began his work, researchers had to look at an entire cloud—they couldn't isolate one particle and watch it grow or evaporate. Ray and his doctoral advisor conquered these limitations by developing a combination electrodynamic balance and laser scattering device. This technology revolutionized the field of aerosol science.

Other applications of Ray's cigarette smoke research suggest a variety of possibilities. One specific result would be learning how to remove undesirable components from the smoke while increasing the desirable ones. Another goal is to use aerosols to selectively control the separation of a component from a vapor phase. An example of this process is the present use of silver iodide to create artificial rain. Particles of the appropriate size and chemical composition are introduced into a cloud. These particles promote the condensation of water on their surface at a lower humidity than normal. This action triggers

the process of forming droplets; if they grow big enough they will fall as rain. Scientists have had limited success with this process.

The pharmaceutical industry is interested in Ray's work too. The goal is to generate a drug as particles which are then inhaled. Based on the size of the particles, the drug would go to certain parts of the body. Patients would benefit because the drug would reach its target more quickly.

Ray is no longer a sole pioneer in his research. Although he's been working with his electrodynamic balance and laser technique for about 10 years, he says it has been only in the last couple of years that many other people have also begun this research. Presently about seven of the 20 major aerosol labs in the U.S. have the device; approximately five are associated with a university. Assisting Ray at UK are nine graduate and two postdoctoral students. Other UK faculty, such as Drs. Len Peters and Tate Tsang, are also conducting research in this area.

In recognition of his accomplishments, Ray has the distinction of being Kentucky's first and only Young Presidential Investigators recipient. Chosen from 2,000 people, Ray was one of 200 faculty nationwide to win in 1984, the first year of competition. His five-year award includes \$25,000 in annual National Science Foundation (NSF) funding; the NSF is also matching up to \$37,500 in grants from industrial sources which, for Ray, have included Brown and Williamson Tobacco Company, Amoco Foundation, and Ashland Oil. The support has enabled him to set up a laboratory, buy equipment, and fund graduate students. "It has given me a tremendous boost in my work, but now I have internal pressure to live up to the award."

Ray sees no end in sight for his experiments. "Since my doctoral work, I have been examining single particles but have developed new technology and expanded the applications. Each time I do something, there are new problems that must be solved. It's a developing thing. Every day we look at the experiments and find the existing theories don't explain them. So we do more experiments and are developing theories as we go."

A STUDY IN ADAPTING

Chemical engineering professor Dr. Asit Ray, a specialist in aerosol science, is not in the field he had chosen as a college student. Nor is he in the area he had chosen in graduate school. Instead, he seems to have had to make the best of a number of plans that went awry.

As a senior in high school, Ray, a native of Calcutta, India, wanted to attend a physics-oriented university in his hometown. But because of campus unrest, admissions to the school were being postponed for several months. Instead of delaying his education, Ray enrolled in the engineering-oriented Indian Institute of Technology in Kharagpur with the understanding that his parents would send in the application to the Calcutta school. However, his parents missed the deadline and he was stuck at the engineering school because, as Ray explains, "it's not possible to transfer like you do here."

After getting his chemical engineering degree in 1975, Ray decided, like many of his friends, to come to the United States to do graduate work. "Everything is so exciting, so many stories," says Ray. He was accepted at Clarkson University (formerly Clarkson College of Technology) in Potsdam, N.Y. Thinking he was going to a big city, Ray was surprised to find himself among a population of 10,000 people, 300 miles away from New York City, a dramatic contrast to his native city of more than seven million people. And none of his friends from India were there either.

"In retrospect I think it was the best thing for me," says Ray. "Being in a small community, I was really exposed to the culture very intimately. I had to get to know them, even if I didn't want to. In a big city, it's easier to isolate oneself."

As a student at Clarkson, Ray received a full fellowship. After arriving on campus, he selected three areas that he wanted to study; his first choice was mathematical modeling but again he got something other than what he expected—his third choice, light scattering and colloid and interfacial phenomena research, which is similar to aerosol liquid sus-

pension research. "I was initially reluctant to get started on my masters," admits Ray.

Yet despite being alone in a foreign country and studying something other than his first or second choice, Ray became adjusted to his new home. He made so many friends that he confesses to having partied too much and to not being productive.

After Ray's second year, his thesis adviser, E. J. Davis, became the chairman of the chemical engineering department at the University of New Mexico. With another full fellowship, Ray went to Albuquerque too. Not knowing anyone except Davis, Ray concentrated on his research. "That first year there was my most productive time during my graduate work, maybe so far even."

In 1980, Ray moved to UK; he had originally planned to accept a position at New Mexico but at the last minute changed his mind. Instead of waiting a semester to begin working at another institution, Ray accepted a UK position negotiated by Dr. Len Peters, then chairman of the chemical engineering department, despite a UK hiring freeze.

"We saw the potential for what he was doing, how unique and novel it was and that he stood at the forefront of his field," says Peters. "It was one of those things where if we didn't act quickly, somebody else would have taken him."

Ray's research contributions have been outstanding but he's modest about his success. "I like what I'm doing and apparently others think it's good work. It's mainly intuitive; I have these hunches about something and so I test it and it comes out." —Lissa D. Atkins

HELPING NEWBORNS TO BREATHE

by Susan H. Donohew and Lissa D. Atkins

"Jimmy" was born too soon. Weighing only 600 grams (1 lb. 5 ozs.), he arrived at 26 weeks, 14 weeks early of being full-term. Today, three weeks later, his eyelids are still fused, and he can't maintain his body temperature. His most serious problems are his inability to breathe and to digest food properly. Five years ago he probably would have died.

Instead he is surviving because of advances in neonatal care, specifically in the use of ventilators and improved formulas. Not all babies,

however, respond to the new techniques; others improve but still develop serious complications. Partially supported by funding through the Infant Intensive Care Program (IICP), the UK Medical Center's three neonatologists: M. Douglas Cunningham, head of neonatology; Nirmala Desai; and Thomas Pauly are finding new ways to treat these infants.

Managing the Neonatal Intensive Care Unit (NICU), the neonatologists treat 650 to 700 premature and full-term infants each year. According

to Dr. Pauly, 60 percent of all the babies have respiratory disorders. For premature infants, their respiratory problems arise from lung immaturity.

"The lung is the last organ to become fully developed in the fetus," says Dr. Cunningham. "When babies are born early, their lungs don't have the mechanical or chemical maturity required to sustain their respiratory needs."

Normally, babies' lungs secrete a substance, surfactant, which keeps the walls of the alveoli from adhering. Surfactant is a mixture of chemicals



that reduces the tension produced when two surfaces rub together. Phosphate detergents have some of the same properties as surfactant. For example, when you wash two smooth glasses—dipping them into water, then stacking them—they're difficult to separate while they're still wet. But, if you mix a detergent with the water, the glasses are easily pulled apart.

Surfactant serves a similar function in the lungs because it allows the lungs to remain pliable. However, this chemical isn't fully developed in the fetus until the 35th week (eight months into the pregnancy), so a premature baby's lungs, lacking this "oiling" substance, are stiff and difficult to open and force air into. The infants have the additional biomechanical liability of thin muscles and a limited energy supply. Hence, the infants need help in breathing to survive.

The full-term babies in NICU, like many premature ones, can be born with or quickly develop a respiratory disease such as pneumonia. The result is that the infants must be helped with oxygen and a ventilator which blows tiny puffs of air into their lungs. A major problem with infant ventilators is that while the baby

must have the air forced into its lungs, that pressure often causes tissue damage. Like an overextended balloon, the alveoli may rupture and allow air to escape into the chest cavity or cause a lung to collapse.

Ventilators for infants were developed in the late 1960s and designed to accommodate 6–8 lb. infants. However, the expectations for the survival of a premature baby have increased dramatically. In the late 1960s, premature babies who survived weighed at least 3–5 lbs. In the mid-to late 1970s, success in saving a 2–3 lb. baby was just short of a miracle. Today Cunningham says, "There's a 90 percent chance of survival for a 2 lb. infant. We even expect a fair chance of survival for a 1 3/4 lb. baby and we expect to save a few of the 1 and a 1 1/2 lb. infants."

A More Delicate Touch Needed

The dramatic decline in the weight of babies who are now surviving has made the 1960s ventilator equipment obsolete for saving these tiny infants. The amount of pressure needed to expand a 6 lb. infant's lungs is considerably greater than what is needed for a 1 1/2 lb. infant. As Dr. Cunningham explains, "The tolerances and capaci-

ty of the lungs of these infants vary greatly."

Cunningham and Desai are developing methods of application for ventilators sensitive enough for use on 1–1 1/2 lb. and larger infants and are establishing a data base so that physicians can more accurately determine the correct setting for the ventilator. Presently, physicians set the ventilators—choosing pressure, amount and rate at which the respiratory gases are administered—based on indirect methods of lung assessment. As Cunningham says, "The state of the art right now is to rely on x-ray pictures of the lungs, blood samples for carbon dioxide and oxygen levels, and an examination by stethoscope. There is no match up with how the ventilator mechanics are set with regard to the actual lung mechanics."

Beginning their work in 1978, Cunningham and Desai spent four years building their own pulmonary function testing device with the help of pulmonary specialist Deborah Mynheir, computer programmer Diane Gagel, and a consultant, Peter Burbank, from the UK bioengineering and medical instrumentation department. The researchers also employed techniques used by the UK College of Pharmacy faculty in pul-

continued on page 16

The NICU babies sometimes weigh as little as 21 ozs.

Left

A NICU baby lies protected in an incubator.

Nirmala Desai, neonatologist, checks the results of a pulmonary function test. Such tests enable neonatologists to more accurately choose the appropriate settings on ventilators connected to infants.



monary function testing of small animals.

"I knew nothing about computers or electronics and my colleagues knew nothing about neonatology, but together we were able to successfully assemble the parts purchased from various companies to reach the minaturization and sensitivity required to study our tiny patients," says Cunningham.

In 1981, the researchers used the instrumentation for measuring lung mechanics on an infant for the first time. The instruments measure air-flow, transpulmonary pressure, intrathoracic and airway pressures, and tidal volume (volume of each breath respired). This information reveals two important mechanical properties of the newborn lung: compliance and resistance. Lung compliance

refers to how inflatable the lungs are and how easily, by elastic recoil, they return to a deflated state; resistance reflects the narrowness of the infants' airways. With both sets of data, the neonatologist can now begin to accurately set the mechanics of the ventilator to match the biophysical properties of the baby's lungs and support their respiratory needs more safely.

Similar instruments are used and research is underway at Columbia University, the University of Miami, Indiana University, and the University of Pennsylvania Children's Hospital. However, the UK instrument is programmed to record the mechanical ventilator breaths, or the spontaneous breaths of the infant separately and provide separate calculations for each breath. Other instruments used

in similar research do not make separate calculations for each but average them together, thus offering less precise data. The UK researchers stress that their breath-to-breath assessments at the bedside enables them to monitor the baby throughout the critical first week of life—the most unique aspect of their research.

Developing the instruments was difficult. The researchers proceeded slowly in working out the difficulties—testing 20 infants by 1983. The first instrument was unwieldy and time-consuming so, in 1984, the team began building a second one. More compact and easier to use, the new equipment again consisted of parts obtained from different manufacturers. To date, with this new equipment, the neonatologists have measured pulmonary functions in more than 100 infants.

During this time, the neonatologists developed guidelines for which patients should be tested and the appropriate time and method for testing so that the ongoing care for the patients was not disturbed. They also correlated the pulmonary function testing results with x-rays and the various disease states. The result is that they have a data base of values for babies at different ages and weights.

The questions being addressed now include the correlation between the improvement of nutrition and the effect of various drugs with pulmonary function testing. The research team is also beginning to use the testing to determine the best time to wean the babies from the ventilators.

Another project for the neonatologists concerns improving the testing equipment. Presently, it cannot be attached to the babies for more than 80 minutes—enough time for only one complete study. Yet "lung mechanics are constantly changing and we can't be continually calibrating and setting



M. Douglas Cunningham, chief of neonatology, examines one of the NICU patients.

Ventilators to help newborns with breathing difficulties were developed in the late 1960s and designed for 6-8 lb. infants. Today there is an excellent chance of survival for a 2 lb. infant so the ventilators have had to be redesigned to be sensitive enough for use on these tiny survivors.

up the equipment each time the ventilators require resetting," explains Cunningham. Rather, he says, they are working toward "real-time" monitoring for the infants with servo-control ventilators. These ventilators would be interfaced between the pulmonary function testing instruments and microcomputers, one which would make the necessary calculations and also automate ventilator adjustments based on those calculations.

"My suspicion is that we overuse ventilators and that some, if not all, of the chronic lung disease of infancy is incurred by them," says Cunningham. "With servocontrol ventilators, the treatment would be safer, more accurate and more effective."

Cunningham says he anticipates the development of pharmaceutical agents that will make up for the chemical deficiency in premature infants that leads to their respiratory problems. They will contain some of the properties found in surfactant and will enable the infant to breathe until its body has matured enough to breathe on its own—without the help of ventilators. Until then, Cunningham, Pauly, Desai and other researchers around the country are buying time for some very sick infants.

THE CHEETAH MODEL

The long-legged cheetah springs forward, racing and bounding in a long chase across the African plain in pursuit of the tawny gazelle. Pounce. The gazelle is dragged down and the cheetah comes to an abrupt halt, savoring his conquest. But he is doing something else too—something more subtle. He is panting—quick short pants—almost a vibrating motion and most certainly a different way of breathing than a marathon runner at the conclusion of a race.

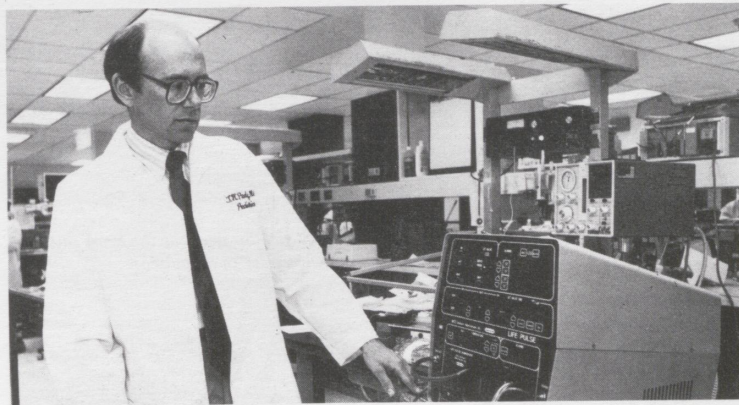
This observation inspired medical researchers to think that perhaps there are other ways to breathe than the ways we normally do. And, for premature infants who have such difficulty breathing, the implications have led to a new approach in ventilators.

Dr. Thomas Pauly, the first doctoral fellow funded through the IICP, returned to UK from West Virginia University last summer. In October, he and physicians from eight other institutions—Children's Hospital of the University of Pennsylvania, Denver Children's Hospital, Primary Children's Hospital in Salt Lake City, Temple University, University of Tennessee, Georgetown University, Louisiana State University, and Jefferson Hospital in Hershey, Pennsylvania—began testing a high frequency jet ventilator.

It, like the cheetah, pants or vibrates—delicately and rapidly. UK's instrument, the only such ventilator in use in Kentucky, breathes at 240-900 breaths per minute compared to 20-80 breaths per minute for a conventional ventilator. It also uses less pressure and may therefore cause less trauma to the lungs. In this two-year study, Pauly has successfully ventilated 12 patients, infants who had failed to respond to conventional ventilators and would have died.

The instrument is used as a "rescue" device because, just as the cheetah can't continue to breathe in rapid pants, the infant also can't maintain the panting stimulated by the jet ventilator. The panting results in the lungs continuing to expand because gas accumulates and is not completely expelled during the short rapid breaths. An infant is, generally, placed on the instrument from eight to 36 hours and then put on a conventional ventilator that provides a more normal type of breathing and complete expulsion of gases from the lungs.

"I think the jet ventilator may have more promise than the conventional ones in the treatment of certain disorders," says Pauly. "But we've only got preliminary data and haven't made any conclusions yet."—Susan H. Donohew



Thomas Pauly is studying NICU infants and the use of high frequency jet ventilators, a machine that forces air into the lungs of babies who otherwise couldn't breathe.



Derrick Deaton sleeps as the heart rate monitor keeps track of his pulse.

INTENSIVE CARING

by Lissa D. Atkins

Even to the casual observer, this hospital nursery is unusual. Although, like any such nursery, there are babies in bassinets dotting the room—proud relatives coming by to visit their off-spring—nurses chatting with doctors—and an occasional laugh interrupting the sound of fretting infants—the similarities with other nurseries ends there.

In the University of Kentucky's Neonatal Intensive Care Unit (NICU), tiny feet and hands do not energetically reach, stretch and poke the air. These tiny babies don't spend the day being fed and cuddled by their mothers. There are no scheduled viewing times when they're brought to a window to be admired by family and friends. They will not be going home in two to four days with their parents.

Instead, these infants stay enclosed in plastic incubators, sheltered from activity. Tubes and intravenous pumps are attached to their arms and mouths to supply medicine, nutrition and oxygen. Nearby, monitors flash data and ventilators force air into the babies' lungs. Dressed in starched white hospital gowns, parents approach cautiously. Some hope that they'll be able to take their baby home in a couple of weeks; others realize that such a homecoming will not be celebrated soon.

These are the sickest infants—about 700 per year—from 61 central and eastern Kentucky counties. These babies come to UK because the NICU provides the best care possible in the region. According to Dr. M. Douglas Cunningham, chief of neonatology, part of the unit's success is due to the Infant Intensive Care Program (IICP).

The IICP began 13 years ago after the passage of the Social Security Act of 1974. The purpose of the act is to

provide federal funds which are matched by state grants to foster and perpetuate infant intensive care. The funding is provided through an annually renewed contract extended to UK from the state Cabinet of Human Resources.

As a supplement to the neonatology department budget, the IICP funding means that UK can offer a complete program for infants requiring intensive care. In 1974, UK had a high risk nursery but not an intensive care unit. The only such unit in the state was at the University of Louisville's hospital. Cunningham, recruited from the University of California at San Diego, joined the UK Medical Center staff to establish UK's NICU. Arriving in Lexington in the summer of 1974, he received approval for the IICP that December.

With just over \$200,000 from the IICP that first year, Cunningham and the other neonatologist, Dr. Nirmala Desai, began adding equipment and personnel. By 1976, the 26-bed NICU was established and a social worker, dietician, respiratory therapist and three doctoral fellows were supported.

Today, the IICP funding—\$462,000 for 1986-87 fiscal year—together with Medical Center support mean that three neonatologists, 87 intensive care nurses and a 45-bed unit are available. Furthermore, a discharge planning coordinator, follow-up coordinator, a transport team, and an administrative staff of 12 are funded. This group of professionals provides the most complete intensive care possible—getting the babies to the unit, treating them, educating their parents, ensuring healthy home environments, and offering post-hospital clinic services.

On the average, the babies stay in NICU for 21 days; although a few are treated in 3 days and others need six months of constant attention. The NICU patients range in age and size from 24 weeks gestation, 600 gram (21 ozs.) premature babies to 40 weeks gestation, 7-8.5 lb. full term infants. Their health problems are numerous and include seizures, low heart rates,



Nurse Judy Hoppin, transport coordinator, arranges transports of neonatal patients for 47 hospitals in central and eastern Kentucky.

and various handicapping conditions. The two most serious and common difficulties are respiratory disorders because of lung immaturity or disease and feeding intolerances because of gut immaturity.

For babies born at UK, moving them to the unit is no problem. However, 50 percent of the NICU patients come from outside of the Medical Center. Helping to get those babies there is the job of a transport team which has access to a private ambulance service and a Military Assistance to Safety and Traffic (MAST) helicopter based in Fort Knox. Begun in 1979, the transport team receives calls from physicians throughout central and eastern Kentucky. After arranging the pick-up time and transportation, the transport takes anywhere from one hour for service in town to 14 hours from Pikeville during bad weather.

From 1979-1981, the transport team was strictly volunteer with personnel available during their off

The nurses have to be very attentive to the infants and sense small changes that aren't reflected in the monitors. For example, a drop in the temperature of the baby's feet is a sign of a worsening blood flow to the extremities.



The bulletin board behind Lisa McGee, follow-up coordinator, shows some of the healthy, recovered children who have spent time in UK's NICU.

continued on page 20

"Parents with handicapped children often don't realize what that handicap means when the baby is small and can be easily carried around."

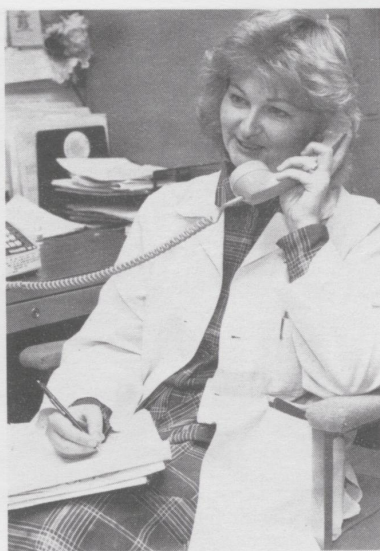
shifts. In 1981, nurses dedicated to transport were hired, although each transport required a physician. In March of 1986, three nurses went through extensive classroom training and worked with doctors on actual transports. With this training, the nurses began what is known as nurse/nurse transport last October. The trained nurses can often handle a transport without the help of a physician.

According to Nurse Judy Hoppin, transport coordinator, the reasons for implementing the advanced nurse transport training were to reduce the load of physicians who were doing transport in addition to their regular work and to provide a challenge and a chance for advancement for the nurses. "Of course, there are still situations when a physician is required, but the nurse/nurse transport has greatly reduced those times." Three more nurses are expected to begin training this spring.

Once in NICU, the babies receive round the clock attention by one of 87 NICU nurses. Caring for one to four infants, depending upon the severity of illness, the nurses are responsible for the infants' minute by minute assessment. This means, for example, that they coordinate the five or six intravenous pumps of necessary medication so that the baby gets the right amount but at a rate of no more than a teaspoon of fluid per hour because that is all the baby can tolerate.

According to Nurse Sally Kinnaird, clinical specialist, the nurses must have "incredible attention to minute details, to sense small changes that are not reflected in the monitors and other objective data." A drop in the temperature of the baby's feet is a sign of a worsening blood flow to the extremities. Other factors such as noise, light, or touch may cause the baby to react negatively.

The nurse has an equally important responsibility to the parents and family. "This is a big crisis time for them and may affect how they perceive the baby for the rest of their life," says



Molly Patchell, Social Worker

Kinnaird. She says the nurses must constantly help the parents defuse the attitudes of having failed, of having been unable to protect their babies, because their expectations of what a baby should look like have been shattered.

"They may think the baby will have blue eyes or blond hair, but nobody expects their baby to be this tiny, critically ill infant hooked to monitors and tubes. Often somebody will say something to the mother like 'I told you you shouldn't have scrubbed the floors at eight months,' which is a devastating thing to say. We're always telling the parents that nobody knows what causes babies to be born prematurely," Kinnaird explains.

To help the parents adjust and begin bonding with their baby, the nurses use a number of strategies. To overcome their fear of handling the baby, parents may wash its face, apply lotion, or change its diaper. The cribs are personalized with name tags, mobiles, cards, and small toys. When the babies are well enough, they have their own blankets and wear their own clothes. These touches help the parents to begin creating positive memories unique to that baby, as

they would do at home. Furthermore, this attention helps make the sick infants seem more like the baby anticipated by the parents.

"The idea is to get them past all their guilt, shattered expectations, and fear so they can focus on the care of the baby," says Kinnaird.

Once the babies are well enough to leave the hospital, staff participation in the IICP doesn't end. Follow up is a very important part of their recovery. "We make sure that every baby who comes through receives health care maintenance," says Lisa McGee, follow-up coordinator. For some babies, this means visits to cardiology, ophthalmology, physical therapy or neurosurgery specialists. Others require CAT scans or neurodevelopment checks.

Each week, about 30 babies are seen for their one year checkup. Babies with more severe problems are seen more frequently. Infants who are healthy and have no problems are referred to a primary care physician with the understanding that the family can call to talk or be reactivated at any time. For those who do not show up, McGee is on the phone making sure the infants are being seen by a physician and the physician is aware of special problems.

Many of the families have little or no resources to care for the baby. Molly Patchell, a social worker at UK, attempts to solve this problem by working with local agencies to obtain formula, clothing, blankets, and baby beds. "I can spend hours making sure a baby has food," says Patchell. A lot of the families don't have phones so finding and communicating with them is difficult. Both Patchell and McGee often rely on the health department or agency in the local community to find the family.

Patchell's counseling work involves a variety of situations. Mothers who are giving up their sick babies for adoption experience a double grief. Support is provided for when a baby dies or is likely to die after a long illness. In other situations, counseling is not needed until after the babies are a

little older. "Parents with handicapped children often don't realize what that handicap means when the baby is small and can be easily carried around," says Patchell.

Other counseling situations may involve discussion of alcohol, drug or child abuse. She says that most families are very open about their problems and estimates that 80 percent of them need physical or emotional support.

Patchell's role also involves representing the family to the staff and doctors, making sure they are aware of any limitations. For example, a doctor may give the family written instructions to follow. But if the parents can't read, these instructions have to be orally communicated. She also speaks to community groups, providing them with information and ideas about ways to help.

The NICU and IICP are working. The NICU mortality rate has dropped from 21.8 percent in 1974 to 9.6 percent in 1986—the lowest rate ever. This rate has declined despite the increase in the number of sick infants and in the severity of illness. From 1974-81 the NICU annually received 500-600 admissions; of every ten babies, three would be critically ill. For the past six years, the unit has been receiving 700 admissions per year with five or six of every ten being critically ill.

According to the neonatologists, the reasons for the increases include better care by local doctors so that the mildly ill babies stay in the regional hospitals and only the severely ill are sent to UK, better techniques for stabilizing and transporting critically ill infants, and better obstetric management so that more babies are surviving who previously would have died.

The neonatologists have another encouraging sign that points to success. Despite the higher number of NICU infants, "studies have shown that with the increased rate of survival, the handicapping rate has not increased," says Desai. "The majority of the babies do well."



Nurse Sally Kinnaird watches Michael Frederick who is recovering well but at 14 weeks weighs only 3 lbs., 15 ozs.

PITCHER SCIENCE

by Jeff Worley

As an undergraduate at Brooklyn College in the late 60s and early 70s, Robert Shapiro would sometimes put his books aside and spend an evening in the bleachers at Yankee Stadium or Shea, watching the best pitchers in the world do their stuff.

He saw Stan Bahnsen go 17-12 for the Yanks in '68 on his way to The Rookie of the Year Award. He watched Tom Seaver post a remarkable 25-7 record in '69, the Mets' pitcher a runaway winner of the Cy Young Award.

Over a dozen years and three academic degrees later, Professor Shapiro found himself face-to-face with Seaver, then with the Chicago White Sox, on a regular basis. They talked about (as one might well imagine) pitching. More specifically, they discussed the biomechanical movements of pitchers, the focus of Shapiro's research project which he is continuing at the University of Kentucky.

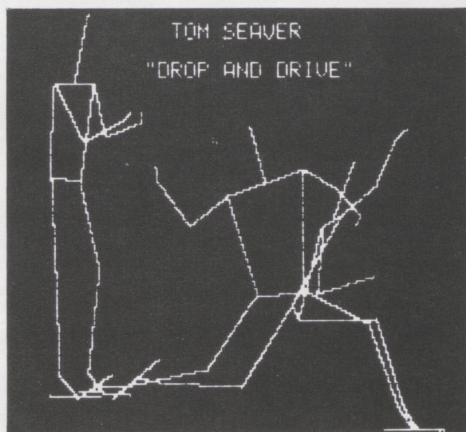
"My interest in the study of pitching styles grew naturally from my lifelong love of baseball and from the work I had done at Penn State and the University of Illinois in Urbana," Shapiro says. His doctoral work in

Physical Education involved intense study and analysis of the biomechanics of batting.

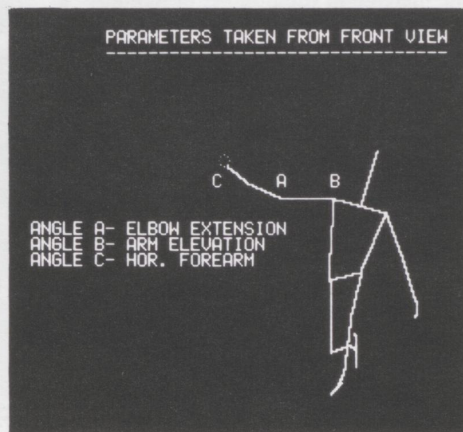
"In 1977, I met with Bill Veeck, club president of the Chicago White Sox. He was very open to the idea of my filming White Sox batters. With the cooperation of General Manager Roland Heman, I began filming that year," Shapiro explained. After analysis of a number of high-speed films of each White Sox hitter, he was able to pinpoint any irregularity in the player's stance and swing at the plate.

Veeck sold the team in 1979 and a new staff was brought in. Since White Sox pitching coach Dave Duncan was so enthusiastic about continuing the project, Shapiro's focus shifted to the filming of pitchers. "I had good access to the team in '83 during spring training," Shapiro says. "I also had an open-ended pass to Comiskey Park, where I took films during the season and analyzed variables for each pitcher. For a kid who always wanted to be a Major League Baseball player, this was a dream come true."

Shapiro would set up his camera in the photographer's booth in the first base or third base dugout in order to be at a 90-degree angle to the pitcher's motion. (Sometimes a research



A digitized computer representation of the pitching motion of now retired baseball player Tom Seaver. From the drawing, a coach can determine various information such as length of stride and knee angle which reveal if the pitcher might be in jeopardy of hurting his shoulder.



This representation shows different angles of the pitching motion and can be used as a guideline for potentially dangerous movements.

assistant would use a second camera in the box seats directly behind home plate). Shapiro used a high-speed camera which recorded at a rate of 250 frames per second so that the different phases of the pitching process could be captured.

"In analyzing the films I could relate the five phases of throwing—wind-up, cocking, acceleration, release, and follow-through—to other bodily movements. I could accurately measure the length of a pitcher's stride to see whether or not his movement was consistent," Shapiro explained.

White Sox pitcher Jerry Koosman was perhaps the chief beneficiary of Shapiro's analysis that summer. As the season progressed, Koosman complained of tiring in the fifth or sixth inning of games he pitched. Based on Shapiro's films, which showed that Koosman's stride during the release phase had gotten longer, the coaches had Koosman shorten his stride so that he would use his legs more during the release and follow-through phases, a change that apparently eliminated some arm strain. Koosman's pitching improved during the remaining weeks of the season.

Since joining the University of Kentucky faculty last year, Shapiro has been involved in a new, more advanced phase—one could say, literally, angle—of this biomechanical research. With funding from the Kentucky Sports Medicine Clinic and strong support from Keith Madison, UK baseball coach, Shapiro has been developing a three-dimensional method for pitching analysis.

"We've taken high-speed film of UK pitchers in order to develop a co-ordinate system for different body landmarks," Shapiro explained. Two cameras, which remain in set locations, are used in order to create a three-dimensional model. The pitchers wear no shirts so that different spots, on the throwing arm for example, can be "marked" during film analysis. Shapiro will then be able to connect lines from various points on the pitcher's body to discover the angles of movement during a pitch.

"What we get are two views slightly displaced that create a stereo depth, similar to what civil engineers do when they create an aerial photograph. This technique, the direct linear transformation method, is a standard 3-D technique," Shapiro pointed out.

After analyzing the films, he will be able to determine how body joints interact and get a clear idea about the forces at the joints. Sha-



piro will then correlate his results concerning elbow and shoulder actions with findings of orthopedic surgeons in order to attempt to discover the causes of certain injuries.

"Doctors who've found a certain kind of tear in an athlete's anterior rotator cuff muscle, for instance, have been able to make only an educated guess about the causes for this damage. What we're attempting to do is to determine what such an injury correlates to in the actual motion of the arm—the causes for the tear," Shapiro explained.

Shapiro says that the results of this research may help surgeons to become more knowledgeable about how bodily joints function and that such information could allow athletes to

continued on page 24

extend their careers. "Years ago, if a baseball player or a swimmer hurt his shoulder, he was finished. Open surgery was required—a surgeon had to make an incision and cut right into the muscle. Now, a surgeon using an arthroscope can make a small puncture in the skin and go directly into the joint cavity to repair a frayed tendon or rotator cuff, allowing the athlete to be back in competition in a month." His findings, in their preventative applications, may help some athletes avoid the operating table entirely.

Another application of the research project pertains to an athlete's rehabilitation progress. In the past it has been difficult to measure to what extent a player has "come back" from an

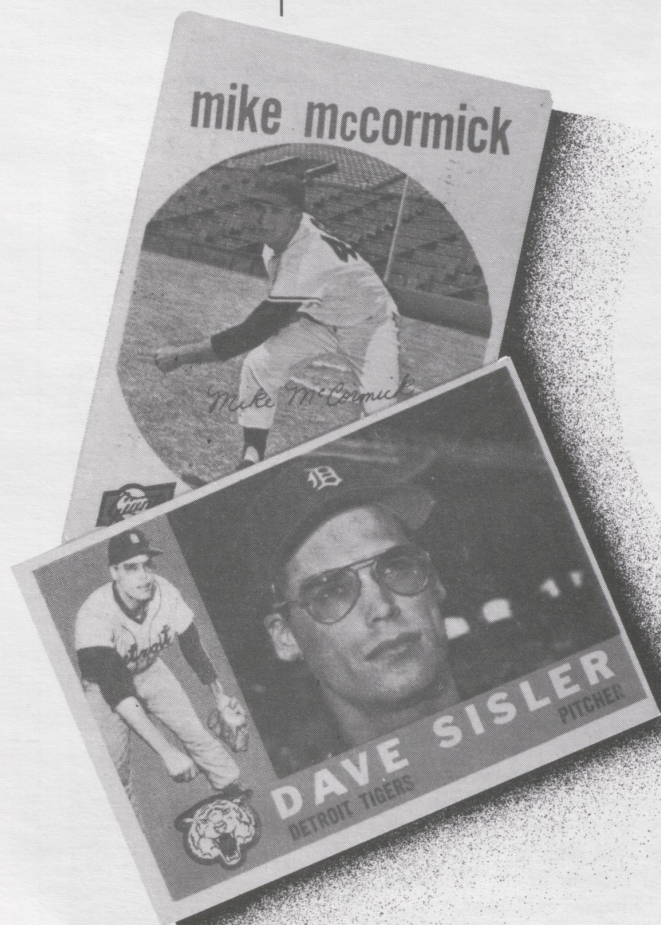
injury. Teams that have films of players in action before an impairment, however, can now more accurately measure rehabilitation because there is an objective record of pre-injury performance. "When professional athletes make so much money, management wants them back; also, since it's not uncommon for players to re-negotiate their contracts yearly, it's in the player's best interest to return to the field as soon as possible to prove he can still play," Shapiro pointed out.

So far, under Shapiro's direction, ten rolls of film have been taken of UK pitchers. Kinetic analysis, which involves numerical measurement of data, began in January.

Because the manual digitizing process is so time-consuming, Shapiro is excited about the possibility of a new high-speed video system which will be used for a wide variety of human and animal studies related to performance and injury. Some components of the system have already been funded as part of the recent \$20 million bond issue. Shapiro says, "This system will track high-contrast 'points,' reflective tape that will be placed over various body landmarks in order to mark pitchers. The computer—which can distinguish among the tape, the player's body, and the background—will do the analysis for us, eliminating hours of manual digitizing." The system is also useful for a variety of other human and animal studies related to performance and injury.

After filming (using three cameras) with this new system in place, Shapiro will be able to show the computer which points to track and which co-ordinates to record. Then, using the three-dimensional algorithm he has developed, the system will take each view and tabulate co-ordinates of all individual points. Shapiro says that the new system should be in place by mid-summer if some needed additional funding comes through.

When research is completed, Shapiro plans to write an article detailing his findings. By that time, baseball will be in full swing; the White Sox may be surging toward the Division title and the World Series. Shapiro hopes so. His pass to Comiskey Park is still good.



WHO MAKES THE CHOICES FOR THE ELDERLY?

by Markel D. Tumlin

"My three daughters and wife . . . They all would have a hand in it," responded an 86-year-old man when asked who would make the decisions about his health care in the event that he became unable to do so for himself. His comment reflects a prevalent attitude of the elderly concerning surrogate decision-making. There are clear-cut choices as to whom they would prefer to have assume the responsibility of their health care. But, according to Dallas M. High of the University of Kentucky's Department of Philosophy, patients

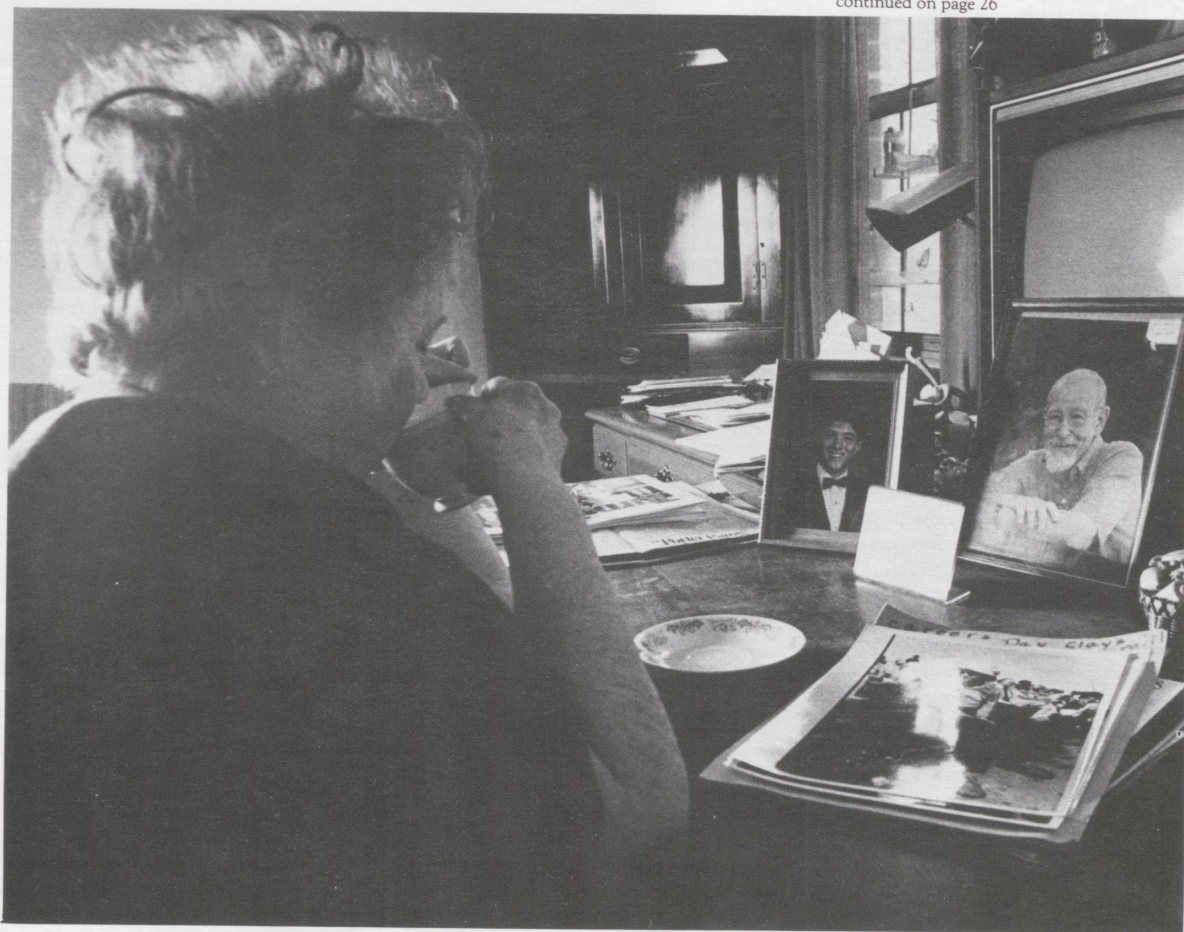
rarely make definite plans concerning the course of their care, and the related laws are not always consistent with patients' preferences. Now that the elderly are the fastest-growing age group in the United States, it is quite likely that these types of issues will take on great significance over the next several years.

Dr. High received a research grant in March 1986 from the Retirement Research Foundation, a private foundation located in Park Ridge, Illinois, to study the options available to the elderly and to make recommendations concerning what changes could be made to increase this group's autonomy. His research is part of the

first phase of a large, loosely knit series of studies being funded by the foundation throughout the United States.

"We used an interdisciplinary approach," says High, whose project included a review of the literature available on the subject, a study of the attitudes of the elderly themselves, and an appraisal of related legal matters. One goal was to discover areas where more research needs to be done. The review of literature included a wide spectrum of published research—philosophical, medical, ethical, theological, and gerontological. Many perspectives on the issue were addressed, and at least one major gap

continued on page 26



in the literature was uncovered. "There's a lot available concerning personal autonomy," High says, "but very little about the part that the family plays in the decision-making process."

High's field research indicates that the role of family members is an area that needs more attention. Aided by graduate research assistant Howard B. Turner, High conducted a series of in-depth interviews with 40 people who ranged in age from 67 to 91. The process of selecting interviewees was aided by services available at UK's Sanders-Brown Research Center on Aging. "We tried, as closely as possible, to mirror the makeup of the general population of people over age 65," High explains.

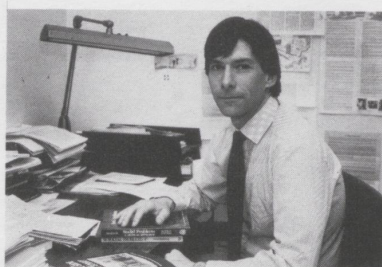
Interview questions centered on what the elderly's expectations would be should they become unable to make decisions for themselves. The UK researchers found that, among the subjects they studied, people generally expect that decisions concerning their health care would be made by close family members, usually a spouse or adult children, in the event that these elderly are unable to do so themselves. A typical response was given by a 76-year-old widow: "I think, really, the way I have lived with my children it would be sort of wrong to appoint somebody besides the family to do these things . . . I am very firm about that."

According to High, these expectations are common regardless of whether or not they have been talked about explicitly with the family. And, in most cases, any discussion on the topic between family members is very casual. Of those interviewed by the UK research team, only 17 percent had put, in writing, any sort of instructions concerning surrogate decision-making.

An exception to this tendency occurs when an elderly person has no family. This individual is more likely to have made definite arrangements concerning future health care. As one 76-year-old widow without children



Dallas High, Philosophy



Howard Turner is a Ph.D. candidate in sociology, specializing in gerontology. He is a native of Stanford, Kentucky.

or siblings summed it up, "That's the reason I had to appoint a power of attorney because I didn't have anybody to make a decision for me." Emphasizing the difference that having a family makes, one man responded, "If my wife died before I do, then I'd have to rethink this thing completely."

A field research discovery that disagreed with one of High's pre-research hypotheses concerned the relationship between decision-making and the geographical distance between family members. "We hypothesized that the greater the distance between family members, the less

likely the potentially incapacitated person would depend on the relative's input into the decision-making process." However, this was not found to be the case. Instead, the researchers discovered that many of the subjects studied expect their relatives (particularly adult children) who live far away to assist in surrogate decision-making. This is true even when the adult child lives several hundred miles away.

The legal component of the research included a review of the state laws of all 50 states. Federal lawmakers generally leave this type of legislation to the discretion of state officials. Assisted by his wife Diane, an attorney, High studied laws concerning the use of advanced directives in surrogate decision-making as well as the important court cases related to the issue. One area researched pertained to the statutory living will laws which 39 states have enacted. High says that, as a result of his studies, he is less of a proponent of such laws because he has found that there are less formal ways of accomplishing the same goals.

High also found that some legal commentators argue against the family's legal authority to become surrogate decision-makers, particularly in cases where there have been no advanced directives or guardianship.

As a result of his research, High has come up with several recommendations concerning the issue of decision-making and also concerning the directions that future research needs to take. He hopes his findings will influence the kind of attention given to the elderly by lawyers and doctors. Additionally, he would like to see the elderly become better educated about their options regarding the planning of future health care.

A second phase of research currently being planned includes a further review of the literature and of legal aspects. Also, more empirical research is in the works. High also plans more interviews with those who participated in the first phase of research as well as interviews with new participants.

SMOKELESS TOBACCO— AN UNSAFE ALTERNATIVE

by Jeff Worley

Mr. Grossmouth is not a pretty sight. An uneven reddish-pink line, like a slow flame burning, covers his gum line. His teeth, those that remain, are a syrupy yellow-brown. Cancer has eaten away part of his tongue and has hollowed out a small crater in his palate.

Although hideous to behold, Mr. Grossmouth (made of hard plastic) serves a purpose: placed conspicuously in front of a classroom of junior high school students, the "model" warns adolescents of the long-term dangers of smokeless tobacco use.

In their research project on smokeless tobacco, Dr. Melody Noland and her associates—professors Richard Riggs, Lea Perritt, Thomas Tucker, Dick Kryscio, and Linda Linville, coordinator of community programs at the McDowell Cancer Network—have been informing junior high and high school students in the Lexington area about the effects of snorting, chewing and dipping tobacco. "Researchers, educators, and public health officials in Kentucky are concerned that smokeless tobacco use among adolescents is increasing. Unless some program of intervention is initiated, many young people will develop a lifelong habit which may present substantial health risks," Noland explained.

She says that since the early 1970s the use of all forms of smokeless tobacco in the United States has greatly increased, especially among children and adolescents. Estimates are that the number of users will double over the next ten years. Why this dramatic increase?

"Fifteen years ago smokeless tobacco was perceived as something only farmers and some baseball players used; now it is marketed successfully to a wider group. It is a fad among young boys and is not difficult for them to get—free samples are often given out at the State Fair in Louisville," Noland says.

Although there has been little research on smokeless tobacco use among children and adolescents, one study found that 13 percent of third-grade males used smokeless tobacco and that this rate increased steadily to 39 percent by grade 11. Smokeless tobacco use is limited primarily to males, although some studies show that 20 percent of teenage girls try smokeless tobacco and two percent go on to regular use.

"A common misconception a number of these kids have is that smokeless tobacco is a safe alternative to smoking. They have been told in school for years how dangerous ciga-

continued on page 28



Smokeless tobacco is now a fad among young boys and is readily available to them.

rette smoking is, but little is said about other forms of tobacco," Noland added.

She goes on to say that smokeless tobacco is detrimental to a person's health in many ways. Usage can result in bad breath, discolored teeth, oral lesions and tooth abrasion. And there is evidence that the chance of oral cancer increases with length of smokeless tobacco use. The circulatory system of the user is also affected: blood pressure ultimately rises, increasing the risk of strokes and heart attack.

With a grant from the National Cancer Institute, Noland and the research team are in the process of conducting a one-year pilot study to identify characteristics of adolescents who use smokeless tobacco and to develop an effective intervention program.

Two of the researchers, Riggs and Perritt, have devised a 12-page questionnaire, a health practices survey with questions that range from a student's beliefs about the health effects of smokeless tobacco to factors that influenced the adolescent to begin using smokeless tobacco.

The questions on the survey are based on the theoretical "Precede Model" of Public Health Educator Lawrence Green, which examines three types of factors to discover an individual's health practices: predisposing factors, which concern the motivation of an individual to act; enabling factors, the skills and resources necessary to perform a health behavior; and reinforcing factors, which determine whether health actions will be supported.

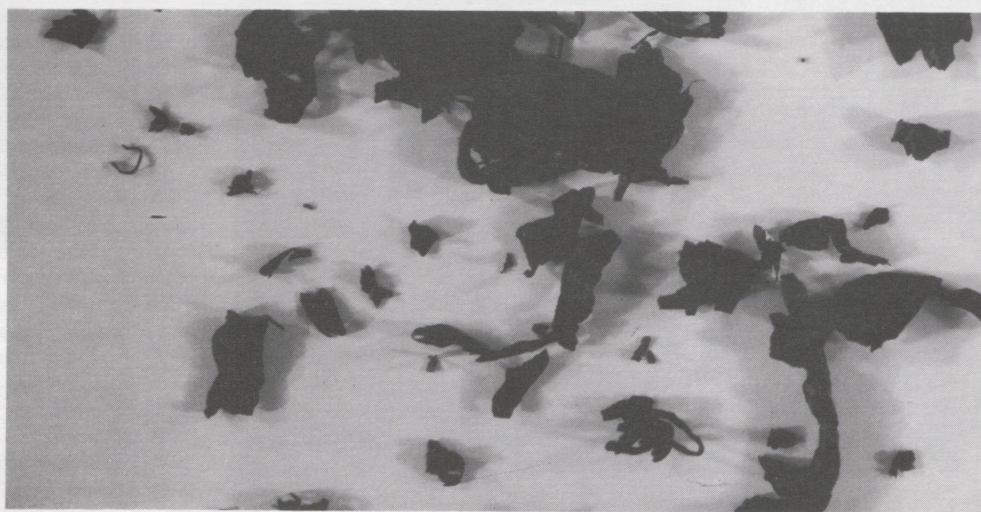
In addition, demographic variables were

included because of their possible impact on the study. "Several studies," Noland says, "have found higher prevalence of smokeless tobacco use reported in rural areas and in tobacco-production areas. Kentucky has not been included in these studies, but since Kentucky has a large number of rural areas and produces a large amount of tobacco, it is likely that the state also has a higher incidence of smokeless tobacco use."

Since the fall of 1986, the researchers have been field-testing the questionnaire. After receiving letters of support from officials in the Montgomery County and Fayette County school districts, Noland and her co-investigators surveyed 1200 male and female students enrolled in grades 7 to 11.

These two districts were chosen primarily because of their demographic differences—the Fayette County School District is a result of the city of Lexington government merging with the county government, while the Montgomery School District is a rural area approximately 40 miles east of Fayette County.

"The administration and faculty in both school districts have been extremely cooperative about letting us come in. We usually stayed in one classroom and surveyed five classes during the day so that the schedule of only one teacher would be disrupted," Noland explained. She and her associates used an overhead projector to preview the questionnaire for students who needed to have words and questions explained. Two of the goals in this feasibility study are to find out how well



the questions are accepted and understood by the students and how the researchers' program works in the classroom.

Part of this methodology, the most unusual part from the students' point of view, involves taking saliva samples from the students. "Each student was given a numbered vial—the same number that appeared on the student's questionnaire— and was asked to fill the vial to a certain mark (2 ml)," says Noland. "There was, of course, some giggling during this process. Sometimes, there were a couple of students, usually girls, who didn't want to spit; the students weren't forced to participate if they really didn't want to."

These samples were then stored in vials, frozen, and sent to the American Health Foundation in New York for analysis of cotinine and thiocyanate levels, tests capable not only of indicating overall tobacco use, but also of differentiating between smokeless tobacco use and cigarette smoking. For detecting smokeless tobacco use, Noland explains, cotinine is the most reliable measure because it detects any type of tobacco usage while thiocyanate will detect only smoking. Therefore, by using both tests, the researchers can attempt to distinguish between smokeless use and cigarette use.

One purpose of this analysis is to encourage honesty in the responses to the questionnaire. A second purpose is to validate the students' responses on the survey concerning tobacco use. "After some of the samples are analyzed," Noland explains, "we can correlate these to the students' responses to see how



The research of, left to right, Melody Noland, Richard Riggs, Thomas Tucker, Lea Perritt, Linda Linville, and Richard Kryscio indicates the use of smokeless tobacco is on the rise among young people. Part of their project involves a three-day intervention program to educate junior high students about the oral lesions, tooth abrasion, oral cancer and other effects from smokeless tobacco use.

many match up. This is a necessary verification process because some of the kids don't respond truthfully—they say they use tobacco when they don't or vice-versa."

All of the completed questionnaires have now been collected, and the results will be analyzed to determine which of the factors of Green's theoretical model predict the probability that a teenager will use smokeless tobacco. Currently, the responses are being coded for computer analysis. Though the complete findings will not be available for several months, the researchers have tabulated by hand the responses from males concerning frequency of tobacco use. At Montgomery County High School, 41 percent claimed to be smokeless tobacco users, while at Tates Creek High School in Fayette County, 17 percent said they used smokeless tobacco either every day or once in a while. At Montgomery County Middle School (7th to 9th grades), 31 percent of the boys purported to be users, compared to 10 percent at Tates Creek Junior High School.

How does Noland account for the greater amount of usage in Montgomery County? "Montgomery County High School is in the middle of tobacco-farming country. Tobacco is a livelihood—part of the community's life style. There is even a tobacco barn on campus where the students in an agriculture course learn the process of curing tobacco."

This demographic reason for the high percentage of tobacco use by these teenagers is only one of several reasons why adolescent use

continued on page 30



One 13-year-old user of smokeless tobacco said that if a small part of his tongue did become cancerous, "that piece could just be cut out."



is increasing so rapidly. Noland suggests a second cause—the media image of tobacco use. "Although there is little hard evidence, advertising probably does contribute to a positive view of use, indirectly creating pressure on young people to use smokeless tobacco," she said. "The actors in smokeless tobacco commercials on t.v., for example, are attractive, healthy-looking people having fun," Noland added.

She suspects that survey results will show peer influence and widespread beliefs about the harmlessness of smokeless tobacco to be other reasons for usage. "Many teenage boys begin using snuff because it's perceived to be the 'macho' thing to do. The peer group also operates under the false impression that smokeless tobacco is risk-free, a safe alternative to smoking cigarettes." Noland recalls a discussion with one 13-year-old user who told her that if a small part of his tongue did become cancerous, "that piece could just be cut out."

The final phase of this project was conducted at Morton Junior High School in Fayette County where a three-day intervention program was taught. A regular teacher at the school and "peer educators," student leaders with strong communications skills, were trained to present information concerning smokeless tobacco, and its short-term and long-term effects. Emphasis was placed on group discussion by the students.

"In our intervention program we included a demonstration with smokeless tobacco, using a college student who regularly chews or dips. Heart rate and blood pressure were measured both before and after the student volunteer used smokeless tobacco," Noland explained. The in-class demonstration clearly exhibited some of the immediate effects of smokeless tobacco use. Noland hopes to test the practicality of this approach and identify any problems associated with it so that in the future such an intervention program can be given as a health unit at the eighth-grade level.

In May the researchers will return to the junior high school to administer the questionnaire again. "This final survey," Noland says, "will allow us to measure short-term changes in knowledge, attitudes, and behaviors which may have resulted from the implementation of the intervention program."

She stresses the need for such research projects that have the direct and immediate result of preventing health problems associated with

tobacco use. "If teenagers understand the potential effects of smokeless tobacco use, some may not try it in the first place. Other obvious benefits are lower health care costs for society and the avoidance of emotional stress for family members who also suffer when the user gets sick."

Chewing Tobacco—loose leaf tobacco found either in pouch or in a plug of compressed tobacco. The "chaw" is placed in the side of the mouth between the cheek and gums.

Dipping—the user takes a pinch of snuff, powdered tobacco, and places it in the gutter of the mouth between the cheek and gums. Locations vary from the front to the side depending upon the user's preference.

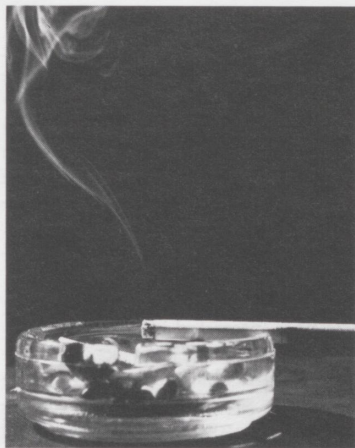
Quid—a small portion of any smokeless tobacco that is held in the mouth for dipping or chewing.

Snuffing—a pinch of finely ground tobacco is sniffed through the nose, a practice more common in England than in the U.S. This form of smokeless tobacco usage is not included in this current research.

SMOKING AND THE IMMUNE RESPONSE

by Maria Braden

SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.



Nobody knows why smokers are more prone to disease, or why they tend to get bronchitis or the flu or other lung infections more frequently than non-smokers.

But a University of Kentucky researcher believes he is on the threshold of finding out. Dr. Mohan Sopori, an assistant professor in the Department of Microbiology and Immunology, says cigarette smoking may affect the ability of the lymph nodes near the lungs to produce antibodies that fight disease.

Using rats as experimental animals, Sopori has found that after smoking for a relatively short time, 20 weeks, the animals show "a very serious loss of immune response." The body's immune response renders harmless invading agents, such as viruses or bacteria, by using white blood cells and antibodies.

Over a longer period of time, 35 weeks—the equivalent of a person smoking for 20-30 years—the rats showed a general decline in the immune response.

Layton Davis, head of the Tobacco and Health Research Institute, says Sopori's research "is an excellent project. It deals with the issue at the center of the smoking and health problem, especially with respect to its effect on the pulmonary system.

"That's what's been missing," Davis continued, "a good examination of the mechanism that leads to the development of diseases . . . We know the risks associated with cigarette smoking, but we don't know the mechanism involved in pulmonary changes and disorders. Once we know this, the next step is to determine what can be done."

Davis says Sopori's results have been encouraging. Sopori himself is even more optimistic. He says he's close to solving the cellular puzzle, and hopes to find the major cells involved in the mechanism within a year.

"Our main aim as immunologists is to establish what happens to the immune response . . . which cells are mainly involved . . . why is the im-

mune system suppressed?

"Immune cells are not a single population. It's a very complex interaction between different cell types," he says. "To find the mechanism responsible for decreased immune responsiveness is a real challenge, but hopefully we should be able to do that. Within the next three to four years we should know how cigarette smoking affects the function of cells in this whole system."

Sopori has been a leader in assessing the effects of cigarette smoke on the pulmonary immune system, according to Dr. Alan Kaplan, Sopori's colleague and chairman of the Department of Microbiology and Immunology.

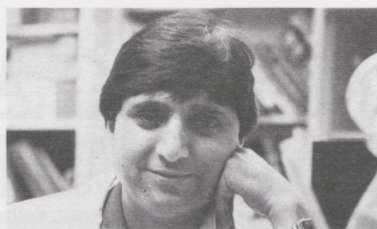
"His particularly unique contribution has been to focus on the lung as a target of immunologic damage," Kaplan says. "In the past, many investigators have evaluated the effects of smoking on the whole organism largely by evaluating the peripheral blood. The results of those studies were mixed because the effects on the whole organism are only seen after prolonged smoking insult."

Sopori undertook a difficult task—to detect how the lung as an immunologic organ fits into the entire immune system, Kaplan says. Little research has been done in the area, partly because it is so hard to get enough lung cells to study. Recent technological advances have made it possible to get cells from the lung, but, even so, the yield is far smaller than with other organs. A mouse, for example, will yield only two million lung cells, compared with some 100 million cells from an organ like the spleen.

Rats, which Sopori uses as experimental animals, yield slightly more tissue than mice. When he first came to UK from Wisconsin seven years ago, he had hoped to use mice in his research, but found that starting a breeding colony was prohibitively expensive. Rats were more readily available, and, as it turned out, proved to be ideal model animals for researchers to use in their study of

continued on page 32

Mohan Sopori, assistant professor in the Department of Microbiology and Immunology, is studying the effect of smoking on the antibody-producing ability of the lymph nodes near the lungs. Within a year, he hopes to identify the major cells of the mechanism involved in the pulmonary changes and disorders found in smokers.



the effects of smoking.

Sopori had not come to UK with the idea of doing smoking-related research, but in his reading on immunology became fascinated with the controversy over the immunologic effect of smoking. "There was lots of literature, yet there were so many arguments," he recalled. "The whole area was very debatable."

Researchers who had used rats had found certain kinds of changes in lung cells similar to what is found in humans, Sopori says. "Since we knew quite a bit about the immune response in this animal, we decided that we should go ahead and could do something [in this area]."

He began by trying to repeat experiments reported by other scientists, a process he describes as initially very frustrating and very difficult. "What was the problem? Why were we not seeing the things that people had reported?"

In humans, researchers had looked primarily at blood cells, since that's usually the tissue easily obtainable from human smokers. He knew that smokers get tumors, but wasn't interested in that aspect since tumors take such a long time to develop and there is no satisfactory animal model system in which smoke induces tumor formation reproducibly.

What struck him was that human smokers are prone to lung infections. He thought there might be changes in the smoker's immune response, but that, in other experimental tests of the immune response of smokers—such as a skin tuberculin test—had turned out normal.

"So on one side, people seem susceptible to infections and on the other the immune response seems fine," Sopori says. He wanted to resolve the contradiction.

In Albuquerque, New Mexico, Sopori got to know David Bice, a researcher who had been looking at the lung's immune response and who had reported that it starts not in the lung but in the lymph nodes associated with the lung.

"We started thinking, 'is it possible that any kinds of changes in the immune response are primarily restricted to the lymph nodes associated with the lung?'" Sopori asked. He went to Albuquerque to learn Bice's technique of depositing antigens in the lung to initiate the immune response. In 1984, he repeated Bice's experiments. The Albuquerque researchers had identified three lymph nodes. Sopori found the fourth. He says the fact that the immune response starts within the lymph node and migrates out into the lung is now well documented.

Currently, Sopori is trying to identify the specific cell type or types involved in the change in immune response. The long-term goal of his studies is to identify the nature of chemical compounds in cigarette smoke responsible for the change—and to see whether those compounds could be altered or removed.

The rats used in Sopori's experiments are obviously not exposed to conditions identical to those of human smokers: the rats are "smoked" in special machines at the Tobacco and Health Research Institute for 10-minute periods daily—what researchers figure is the equivalent of a person smoking a pack of cigarettes over a 12-hour period. "This is the closest we can get, given the constraints of our experimental system," Sopori says.

But the experimental system has been vastly improved just within the last couple of years—an advance which has enabled both Sopori and Kaplan, who uses mice in his research—to make more accurate measurements. The development of improved smoking machines at the Institute—what Kaplan calls "non-invasive" machines—has enabled researchers to "smoke" their experimental animals in "a highly reproducible manner," Kaplan says.

"The Institute has been a great help," according to Kaplan. "It's partly because of them and the facilities that (Sopori) could do work that oth-

Within the next three to four years researchers should know how cigarette smoking affects the function of cells in the immune response system.

ers tried and failed to do."

The highly sterile environment that the rats are kept in at the Institute has allowed Sopori to see how they react after a long period of smoking—50 weeks or more. They have been able to maintain the animals for the last three years without any of the viruses that often affect rats and mice. Sopori hopes to increase the experimental period to 80 weeks.

One of the spinoff research projects he is interested in involves smoking the rats for 35-40 weeks, until the most intense changes in the immune system are seen, and then to stop exposing them to cigarette smoke. Will their immune response return to normal?

Another related project that interests him involves studying the effect of cigarette smoking on reducing stress. Sopori has found a "very significant increase" in endorphins—hormones produced by the brain that make people feel better—in animals that have smoked.

"I don't know what it means . . . but I feel that it's possible that people smoke because they get pacified," Sopori says. "People might laugh at me, but cigarettes calm you when you're agitated . . ."

Sopori also wants to look at the effect of passive smoking—exposure to the cigarette smoke of others—on the immune system and his experimental system is already in place. Animals breathe smoke mixed with fresh air on a delayed basis. This procedure is called "sidestream smoking."

Sopori's research is supported by grants from the National Institutes of Health, the Council for Tobacco Research and the Tobacco and Health Research Institute.

HELPING TO BREAK THE HABIT

by Maria Braden

Dr. Philip Moody, who with Dr. Doris Wilkinson received a National Cancer Institute contract last fall to study cigarette smoking behavior, recalls that a similar proposal he made three years ago was turned down. One factor he attributes to this proposal's success is the involvement of Dr. Wilkinson in the project.

Wilkinson, a medical sociologist, came to the University of Kentucky in 1985. Within two months she and Moody, also a medical sociologist, had begun work on a new proposal for NCI, aimed at preventing smoking-related cancers.

Five months of intense work paid off. They submitted their proposal in February 1986 and in September, Moody and Wilkinson received the \$1.7 million five-year NCI contract to study smoking behavior and smoking cessation programs and to develop their own interventions. They are now in the pilot phase of the project.

Their proposal came in response to a call by the National Cancer Institute for projects that would focus on certain populations—Hispanics, Blacks, women and others—in terms of smoking-related cancer incidence and cancer mortality. Wilkinson told

Moody she thought they should respond.

Moody attended a meeting in Atlanta in December 1985 for researchers interested in making proposals to NCI. "From then on, I saw Phil every day," Wilkinson said with a laugh. "After he came back we talked and mapped out strategies. We worked very, very hard, from October to February, intensively for five months. It was not easy to do."

While their research focuses on smoking cessation in black smokers, Wilkinson said it would have implications for smoking behavior in other groups. It should also provide a data base that could be used to predict who is likely to stop smoking.

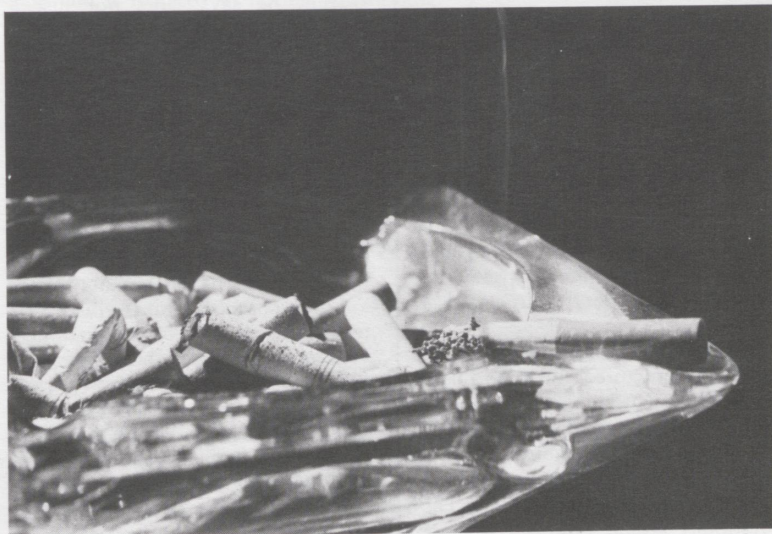
The purpose of their project is threefold: to develop a strategy for recruiting black smokers into a smoking cessation intervention program and maintaining them as nonsmokers for 18 months; to evaluate the immediate and long-term (18 months) effectiveness of two smoking cessation intervention programs; and to develop smoking characterization and attitude profiles of volunteer smokers.

"The focus of the proposal is the primary prevention of smoking-attributable cancers in black populations in Kentucky," says Wilkinson, "but it has ramifications among any populations."

The project should produce useful results says Dr. Gary King, a medical sociologist at WESTAT, Inc., a private survey research firm in Rockville, Maryland. King received a five-year NCI contract to provide technical assistance and to monitor the various smoking cessation projects. "It is one of the more valuable projects, in the sense that it's going to provide a lot of data that we need," he says.

King says the "smoking profiles" of black smokers that will be developed by the UK team will help predict health risks: "No one really has that data. No one knows if (various smoking characteristics, such as puff duration or puff frequency) are contributing factors in blacks."

continued on page 34





Philip Moody, Behavioral Science.



Doris Wilkinson, Sociology.

To measure smoking characteristics and compile a smoker's profile, the UK researchers will use a computer-based machine called a pneumotachograph. A person smokes a cigarette placed in a three-inch long plastic holder which is connected to a pressure transducer. This transducer senses how many puffs a smoker takes, how long each puff is, how much time is taken between each puff, and the volume of the smoke/air mixture a smoker inhales. The transducer is connected to a computer which records the data. The device was first developed by Dr. Robert B. Griffith, former director of the UK Institute of Tobacco and Health Research.

Moody says the smokers' profiles will be used analytically, to determine if they predict success in smoking cessation. They will not be used in the smoking intervention programs. "We are trying to find out if how people smoke (indicated by smokers' profiles) is a predictor variable in who is likely to quit."

Moody has been studying smoking behavior since the early 1970s, and has published work outlining the differences in how people smoke. According to King, Moody's work with the sophisticated pneumotachograph was an important factor in securing the NCI contract.

A second part of the project involves a two-pronged treatment strategy for intervening, using the American Cancer Society's FreshStart program and one Moody and Wilkinson developed themselves, called the Social Support Group. Wilkinson says they created their approach on the basis of the theoretical literature in social psychology and in sociology, and are interested in subjecting the theory to an empirical test.

The Social Support intervention will be unstructured and will involve an individual using "significant others" to help control his or her smoking. The Moody/Wilkinson program involves an individual using others to help control his or her smoking. The FreshStart group, however, is more

organized or structured, using a facilitator to direct interaction about smoking behavior.

A third objective of the project is to find effective ways to recruit special populations, such as low-income persons or blacks, into smoking intervention groups. In such groups, the persons learn about smoking and its effect on their health and about self-discipline since they are required to quit smoking.

In their first year the two researchers are refining protocol procedures, establishing a smoking cessation office in Louisville, hiring personnel, developing reporting forms, and finalizing questionnaires. They are also putting together a state-of-the-art pneumotachograph. They will utilize the smoking machine and begin studies on volunteers to refine their questionnaires.

The UK project is one of six in the nation funded by NCI that focus on smoking behavior. King says investigators from the various projects will be collaborating and are meeting regularly to exchange ideas and data. He says the two UK researchers have a great deal of expertise in their areas and that, working together, they are an impressive combination.

Their project goes beyond pure research, he says: "It's not just a research project—it's more that that: it's research and intervention."

The American Cancer Society's smoking intervention program has not been as successful with blacks as whites, and King says that the strategies proposed by the UK investigators appear "very interesting and useful."

For their part, Moody and Wilkinson hope that what they find will have implications for smoking behavior in other population groups and for the effectiveness of smoking intervention programs, such as their own Smoking Support Group.

"We're hoping to make generalizations to the larger population from the sample we study," Wilkinson says. They also hope their research will have implications for understanding other types of substance abuse.

WALKING TALL

"Which animal walks on four legs in the morning, two legs in the afternoon and three legs at night?"

the riddle of the Sphinx

The answer is man.

by Pam Fahey

The riddle of the Sphinx may no longer hold. It may be circumvented because of what we know today about calcium.

It is not a foregone conclusion that man will only walk in later years with the aid of a cane. Because we understand more today about calcium and such crippling maladies as osteoporosis, much can be done to prevent this awful disease.

In the recent past there has been a lot of popular publicity on osteoporosis—the condition which is held responsible for the stooping posture and crippling of older Americans, especially women. Actually, osteoporosis is an abnormal porosity or rarefaction (becoming less dense) of bone. Hip bone and spine are particularly affected by this condition, which may account for the high incidence of fractures of these bones in older persons.

What happens to make the bones vulnerable to trauma involves calcium. It is known that calcium is moved within the body. It comes from bones when needed elsewhere in the body and is replaced in normal functioning. This whole process involves several hormones, especially 1.25 dihydroxy vitamin D₃, the biologically active form of vitamin D. Without the normal hormone status, calcium alone will not repair or heal bones.

Based on current popularization of osteoporosis research, many people, particularly women, are advised to take calcium supplements to protect themselves against this disease. Yet, taking supplements may be counter-productive.

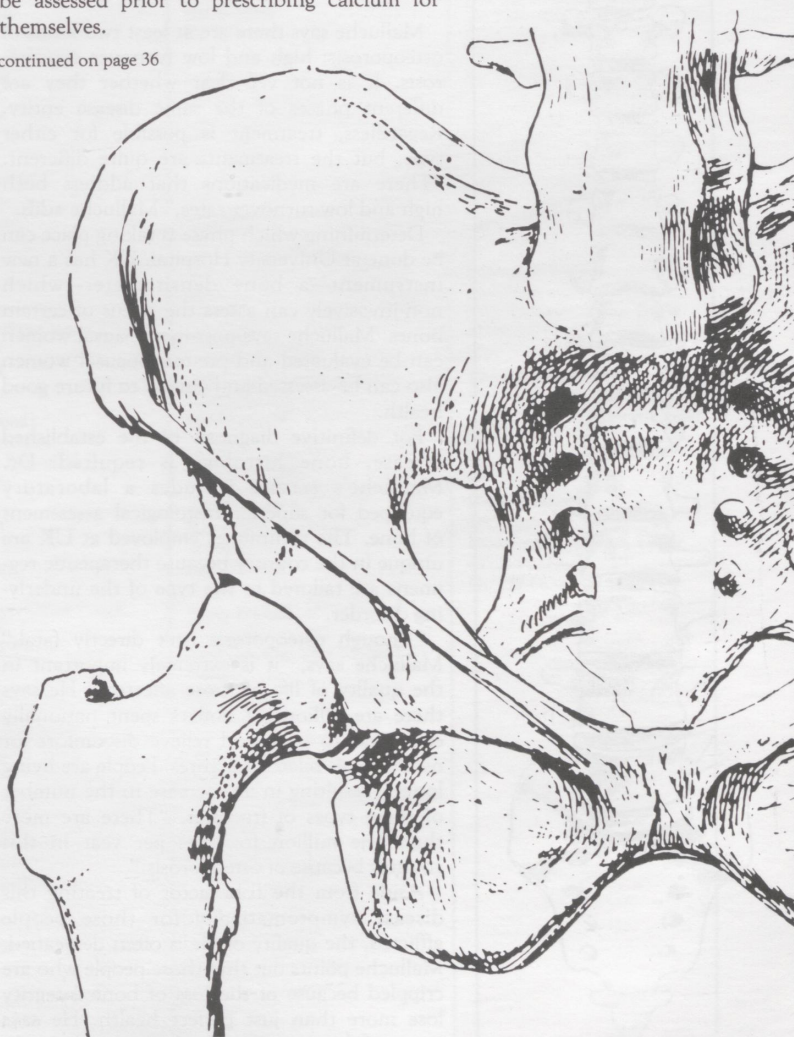
According to Dr. Hartmut Malluche, professor of medicine at the University of Kentucky Chandler Medical Center, and director of the Division of Nephrology, Bone and Mineral Metabolism, "A calcium load will suppress the production of 1.25 vitamin D₃, which is necessary for the normal maintenance of skeletal function." He also says that too much calcium in the diet can be related to

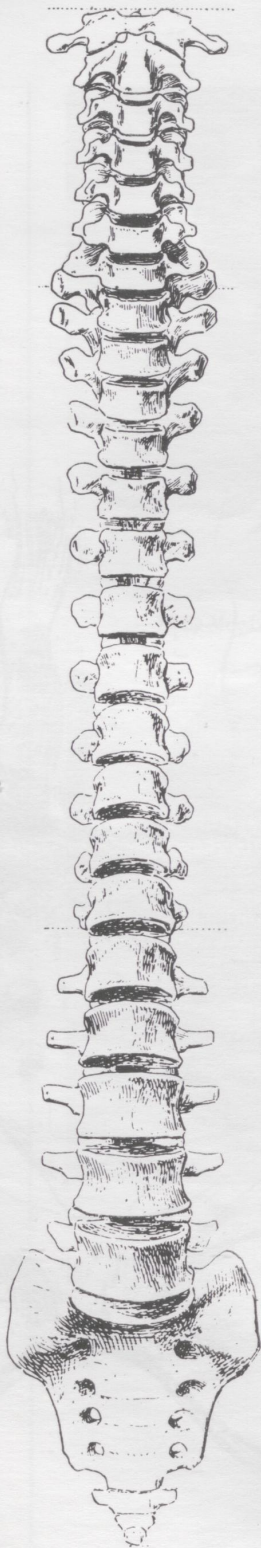
kidney stone formation since many of those stones are comprised of calcium.

He adds that bone density can be increased during the formative years, so calcium-rich diets are important for youngsters. After an individual reaches maturity, though, calcium can only be replaced in bone tissue when the proper hormones are in balance.

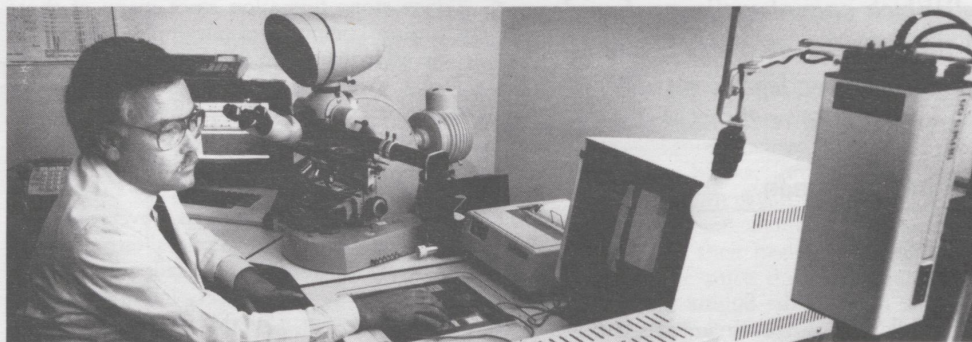
Post-menopausal women, however, are a distinct case. Dr. Malluche says estrogen, the female sex hormone which falls progressively after the menopause, is very important in the 1.25 D₃ story. It is at this point that women may benefit from supplementation, but should be assessed prior to prescribing calcium for themselves.

continued on page 36





There are more than one million fractures per year in the U.S. because of osteoporosis. Funded by a six-year National Institute of Health grant, Dr. Hartmut Malluche is studying the pathogenesis of bone loss after cessation of ovarian function and new avenues for therapy.



Malluche says there are at least two kinds of osteoporosis: high and low turnover osteoporosis. It is not yet clear whether they are different phases of the same disease entity. Regardless, treatment is possible for either type, but the treatments are quite different. "There are medications that address both high and low turnover rates," Malluche adds.

Determining which phase is taking place can be done at University Hospital. UK has a new instrument—a bone densitometer—which non-invasively can assess the status of certain bones. Malluche says post-menopausal women can be evaluated and pre-menopausal women also can be assessed and guided to future good health.

For definitive diagnosis of the established disease, bone histology is required. Dr. Malluche's service includes a laboratory equipped for superior histological assessment of bone. The techniques employed at UK are unique in the country because therapeutic regimens are tailored to the type of the underlying disorder.

"Though osteoporosis isn't directly fatal," Malluche says, "it is extremely important in the quality of life of those affected." He says there are billions of dollars spent nationally each year to treat and relieve discomfort for osteoporosis-related fractures. People are living longer, resulting in an increase in the number of these types of fractures. "There are more than one million fractures per year in this country because of osteoporosis."

Aside from the cost factor of treating this disease symptomatically for those people afflicted, the quality of life is often demeaned. Malluche points out that those people who are crippled because of the loss of bone integrity lose more than just perfect health. He says many of these people are relegated to being in

the care of others. He says for a person who has lived a full, active life, losing that freedom is devastating and demeaning.

"And if this is preventable," Malluche says, "why should we allow it to continue happening?" He adds that University Hospital is the only hospital in the Lexington and Louisville areas that is equipped with the full spectrum of diagnostic and therapeutic methods for osteoporosis.

Malluche also says people can do a lot to help themselves prevent this crippling disease. He emphasizes the need for moderation. "Without sounding like a preacher," he says. "I instruct any patients I see, and I talk with medical students and residents.

"It has become quite an American trait, and it is spreading to other countries as well, to consume copious amounts of protein and salt in the diet. Moderation is the Key! What these protein and/or salt over-indulgers don't realize is that when protein or salt intake is dramatically increased beyond what is necessary for functioning, calcium is lost in the body. We don't totally understand why this happens, but it does."

He also stresses the importance of moderate exercise, a balanced diet—without excesses in alcohol, salt, protein or calcium—and avoiding deficiencies in one's diet, such as those found in many austere weight-loss diets.

Malluche adds that he would like to see physicians prescribe assessment on a routine basis. He says that women traditionally are advised to have a gynecological exam and that he would like to see an osteoporosis-prevention screening exam become part of that regimen.

Malluche's research is supported by the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases.

Directory
University of
Kentucky
Lexington,
Kentucky

Addresses of UK faculty,
staff and graduate stu-
dents featured in this is-
sue of **ODYSSEY**.

Area code is (606)

Peter Burbank
Biomedical Instrumentation
D79 Chandler Medical Center
40536-00849
Ph. 233-5009

M. Douglas Cunningham
Pediatrics
MS472B Chandler
Medical Center
40536-00843
Ph. 233-5366

Layton Davis
Tobacco & Health Research
Institute
Room 200 Cooper &
Alumni Dr.
40506-0236
Ph. 257-2816

Nirmala Desai
Pediatrics
MS469 Chandler
Medical Center
40536-00843
Ph. 233-5541

Andy Feldhaus
Biological Sciences
101 Morgan Biological
Sciences Bldg.
40546-02251
Ph. 257-3804

Diane Gagel
Computer Services
MN104 Chandler
Medical Center
40536-00842

Boyd Haley
Biochemistry
MCC45 Markey Cancer Center
40536-00840
Ph. 257-4481

David Hammond
Biological Sciences
101 Morgan Biological
Sciences Bldg.
40546-00251
Ph. 257-3804

Dallas M. High
Philosophy
1435 Patterson Office Tower
40506-00270
Ph. 257-3071

Judy Hoppin
Nursing Services
H437 Chandler Medical Center
40536-00843
Ph. 233-6683

Alan Kaplan
Med. Microbiology
& Immunology
MS409 Chandler Medical
Center
40546-00840
Ph. 233-8966

Sally Kinnaird
Nursing Services
H188 Chandler Medical Center
40536-00843
Ph. 233-6835

Dick Kryscio
Statistics
823 Patterson Office Tower
40506-00270
Ph. 257-4064

Judith Lesnaw
Biological Sciences
122 MultiDisciplinary Res. Lab.
40546-02251
Ph. 257-3804

Linda Linville
McDowell Cancer Network
167CC Markey Cancer Center
40536-00931
Ph. 233-6541

Hartmut Malluche
Med/Nephrology
MN 572 Chandler Medical
Center
40536-00847
Ph. 233-5049

Lisa McGee
Nursing Services
C419 Chandler Medical Center
40536-00843
Ph. 233-6469

Philip Moody
Behavioral Science
105 College of Medicine
40536-00861
Ph. 233-5716

Daniel Nelson
Political Science
1641 Patterson Office Tower
40506-00278
Ph. 257-7031

Melody Noland
Health, PE & Recreation
202 Hlth, PE &
Recreation (Seaton)
40506-02191
Ph. 257-4265

Molly Patchell
Pediatrics
MS472A Chandler Medical
Center
40536-00843
Ph. 233-8988

Thomas Pauly
Pediatrics
MS467 Chandler Medical
Center
40536-00843
Ph. 233-5530

Lea Perriitt
Allied Hlth Ed. Research
3 Med Cntr Annex 3
(763 Rose St.)
40536-02181
Ph. 257-5418

Leonard Peters
Graduate School Research
106 Kinkead Hall
40506-00057
Ph. 257-8288

Asit K. Ray
Chemical Engineering
161 Anderson Hall (Tower)
40506-00461
Ph. 257-7990

Richard Riggs
Health, PE & Recreation
204 Hlth, PE, &
Recreation (Seaton)
40506-02192
Ph. 257-3645

Robert Shapiro
Health, PE & Recreation
201 Hlth, PE, &
Recreation (Seaton)
40506-02191
Ph. 257-7904

Mohan Sopori
Microbiology & Immunology
MS408 Chandler
Medical Center
40536-00840
Ph. 233-5054

Howard B. Turner
Sociology
1515 Patterson Office Tower
40506-00277

Thomas Tucker
McDowell Cancer Network
CC166 Markey Cancer Center
40536-00931
Ph. 257-4582

Doris Wilkinson
Sociology
1535 Patterson Office Tower
40506-00277
Ph. 257-6878



ODYSSEY

University of Kentucky Research Foundation
Kinhead Hall
University of Kentucky (0057)
Lexington, Kentucky 40506

BULK RATE
U.S. POSTAGE
PAID
PERMIT NO. 51
LEXINGTON, KY.



In this issue:

A Revolutionary in Aerosol Science
Superpower Semantics
Pitcher Science
Helping Newborns to Breathe
Smoking and the Immune Response