Henry L. Bramlette was honored upon retirement by the naming of the neurology research animal complex. Bramlette served as animal handler and technician in the Department of Neurology and Neurological Surgery for 32 years. He was involved in hundreds of research projects and is best known and loved for his way of instructing and advising resident surgeons and research fellows in the handling and care — including anesthesia, surgery and post-operative care — of research animals.

William Landau, M.D., professor and co-head of the department with Sidney Goldring, M.D., both announced the naming at a reception for Bramlette on March 5. Scores of tribute letters were sent to “The Duke Of McMillan” from neurosurgical and neurological alumni throughout the country.
OUTLOOK MAGAZINE

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ALUMNI RECEPTIONS
April 18
Missouri State Medical Assoc. — Crown Center — Kansas City.
May 5
American Psychiatric Assoc. — San Francisco Hilton
May 10
American Society for Clinical Investigation — Washington, D.C. Sheraton

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Apology
The Summer 1979 issue of OUTLOOK Magazine carried an article
entitled "A Quiet Revolution in Childhood Cancer." Recently, an investiga-
tion has disclosed that this article was based, in large measure, on an article
by Susan Schiefelebein, "Children and Cancer: New Hope for Survival,
which appeared in the April 14, 1979, issue of Saturday Review. Portions of
Ms. Schiefelebein's excellent article were used verbatim, and other por-
tions were paraphrased. OUTLOOK Magazine deeply regrets that the pre-
vious editor did not arrange appropriate permission and credit with Ms.
Schiefelebein and Saturday Review prior to publication.
This error in no way reflects on the high standards or outstanding
contributions of Washington University School of Medicine or St. Louis
Children's Hospital in the treatment of childhood cancer. The basic premise
of the article in OUTLOOK Magazine is accurate and unquestioned:
"Washington University scientists and physicians at St. Louis Children's
Hospital are on the front lines of medical research and have played a signif-
icant role in the development of new treatments for childhood cancers."
Nevertheless, a serious error in judgment was displayed by the author of
the article in OUTLOOK Magazine in utilizing substantial sections of the
property of another magazine to describe the work of WU scientists and
staff. For this disregard of accepted journalistic and publishing ethics by
the previous editor, OUTLOOK Magazine apologizes to Ms. Schiefelebein,
to Saturday Review and to you, our readers.
The Blue Bird Cafe has sat on the corner of Tireman and Beechwood Avenues in West Detroit for almost 50 years. Built after the repeal of Prohibition and near the end of the Depression, the small brick nightclub has become an historic fixture in the primarily residential neighborhood. And like its surroundings, the cafe has weathered many changes. Today, a jukebox replaces the bands that used to perform live there, and the glossy dance floor is now covered with tables. It was there, in 1935, that Phillip Venable met Ethel Waters.

Venable, WUMS clinical professor of ophthalmology, was a singer and trumpet player in a five-piece band performing at the club. It was one of many small jobs or "gigs" he took to earn money while attending Wayne State University in Detroit. He was then a 22-year-old college senior with high hopes of enrolling in medical school. Appropriately enough, his nickname was "Doc."

Venable was performing in the 30-minute-long floor shows at the club. During the shows, the tempo of the music changed and the dancing stopped. Patrons would order drinks and send waitresses up to the bandstand with requests for songs wrapped in dollar bills. That was the sort of night it was when Ethel Waters and her agent came to the Blue Bird Cafe — the night when Venable almost declined her request and stunted a musical career, begun with her and continued under Duke Ellington, that would eventually help pay his way through medical school.

"I was in the floor show, singing a few tunes when the waitress came up to me and said that there was a lady in the audience who wanted to know if I knew..."
Medical Career Based On Blue Notes, Not Bank Notes.

Of, Sharps, Flats and Ophthalmology — Dr. Philip Venable, trumpet and vocals with Ethel Waters and Duke Ellington.

'Sylvia.' Well, I said 'sure,' but asked if the lady sent up a tip. She hadn't. In those days you sang for tips. No tip — no song. It was as simple as that," Venable recalls.

"But the waitress insisted that I ought to sing the song. So I sang it and the lady called me back to her table." The lady was Ethel Waters. "Well, I knew she was in town, but I didn't know she was in the nightclub."

Waters and her revue were appearing at the Granada Theatre in Detroit when she, her agent and another member of the revue went out "slumming" after a Sunday night performance. They were out "just having a little fun" when they arrived at the café, says Venable. "That must have been about April 1935."

Waters was impressed with Venable and said that she was thinking of adding a back-up singer to her group for the summer to perform on boat excursions up and down the Hudson River, and for various groups, dances and theatres in New York City. The singer she had in mind was Venable and he was flabbergasted."

Waters auditioned other singers "but most of them didn't know 'Sylvia'" says Venable. "It's a classical tune the average dance man doesn't know." It was also her favorite song.

"Ethel used the song to determine the quality of your voice and its range — it started on C and ended up around A. It's a difficult song, but a song by which you can judge a person's voice. It shows range, diction, breathing and phrasing." Luckily, Venable's four years in the university's glee club and symphony had increased his repertoire of music to include religious and classical selections such as 'Sylvia.'

The hook was baited and Venable was interested, but the job sounded too good to come true. "In music, you hear so much of that, of people offering you a job that never materializes. You get to the point that you become a Doubting Thomas. I had offers like that before, but with other bands, and that was the last I would hear from them," says Venable. "And I was trying to get into medical school, although I didn't hold much hope of that because of discrimination. They had only one Negro at Wayne's medical program. Upon hearing this news, he raced down to the school "to accept their offer, put money down and enroll before they could change their minds."

Two days later, he received a contract in the mail from Waters to join her revue.

Within three weeks, Waters left Detroit on a train bound east, for the soaring skyline of Manhattan, in a city teeming with jazz. It was the beginning of a long trek for Venable that eventually would lead him to the Paramount on Broadway, the Cotton Club on Lennox Avenue in Harlem, and various nightclubs skating 52nd Street.

But the 637-mile train ride left Venable, the son of a Detroit chauffeur and his Canadian wife, a barber, filled with uncertainty. "I wasn't really convinced I had the position or that Ethel would say she even knew me," recalls Venable. "Things like that had happened."

His doubts diminished when he was met at the station by Waters' agent who quickly whisked the musician off to a rehearsal in the basement of a building owned by Waters at 113th and Morningside.

"Once I got there, all my fears disappeared," recalls Venable. "I met the fellows, played my trumpet and sang some songs Ethel had left for me. They were amazed to hear that a man who was going to be in the band was also going to medical school."

Rehearsals were frequent and matched in their intensity by the drive for perfection. "At the top, you can't make a mistake — not even one note, because the public demands perfection," says Venable. "There is no room for error."

"We practiced at 113th and Morningside till we almost dropped dead. I wondered how I was going to have anything left for the evening. But you have to be as perfect as you can be, and that means you have to practice — practice 'til your horn is almost a part of you,' or until delivery of that song is as smooth as velvet and sung with as much gusto the hundredth time as it was the first."

"At first, I became disillusioned when I saw the tremendous amount of practice that they had to do," says Venable. "I didn't dream they practiced so much."

With the bands in Detroit, Venable had "practiced one to two hours a week and we thought we had it made, but in New York we practiced five to six hours a day and then performed. I didn't know if I could hold up under all of that."

But Venable did cope with the pressure and practices, aided primarily by his ability to sight read music readily. "In those big bands, you had to read music because you didn't have much to get ready. We rehearsed in the morning and performed in the evening. They threw that music at us and we had to know how to read it," he recollects. "I could read practically anything in sight but I found out a lot of fellows couldn't. Oh they could — but after three or four rehearsals."

"Because of his anticipated profession, Venable became a surrogate physician and, as such, 'Doc' became an accepted member of the revue. "I became their friend because I knew the answers to a lot of their questions about aches, pains and other discomforts. In other words, they didn't look at me as competition. I was just there for the summer and that made a difference. Besides, the music profession wasn't in full swing in summer. The big stuff came in October and lasted through May."

Venable performed with Waters and her revue for two months, hitting bigtime at the Capital and Paramount movie theatres. "The Paramount was big stuff then," says Venable. "That's where Frank Sinatra got his start."

Waters and her revue appeared at the Paramount for "a week or two," recalls Venable. "We did seven shows daily, each lasting one and one-half to two hours. In those days, the show was the thing, and the movie incidental. People came for the floor show."

At the better movie theatres, the floor shows were a dash short of being a Hollywood production and the Paramount, to say the least, fell comfortably within this range. Band members were suited in pressed uniforms and had the polish of the military about them, with each person strategically placed for the best visual and melodic effect upon the audience. At the Paramount, the band assembled on a plat-
form in a pit in front of the stage and below floor-level. When the production was ready, the platform was raised with all members posed for action like wax figurines waiting to be brought to life by the magic wand of the conductor.

Although he was an accomplished trumpet player, Venable was instructed by Waters to hold the instrument and not necessarily play during a performance. "In those days," says Venable, "there was a lot, shall we say, effect," and not all band members were musicians. Many of them would finger their instruments but never blow a note or strike a chord. Their appearance was enough. "Just to have four trumpets sitting on a bandstand looked beautiful from the audience's point of view." and if one of the four trumpets wasn't being used, the audience wouldn't know, especially if the other three were blaring away. "But if you would hit a wrong note, they would know," says Venable.

"Anyway, Ethel wanted me for my singing, and you've got to have your wind to sing."

Waters would make a few appearances during each show, but the bulk of the performance was left to Venable. "The fellows used to kid me about that. They would say, 'The only difference between you, Doc Venable, and Ethel Waters is that you sing a thousand songs for one dollar and she sings one song for a thousand dollars.'"

But his stint with Waters paid off in experience, public exposure and formal introductions. That summer, Waters introduced Venable to Duke Ellington, who, by that time, was firmly established as a kingpin of jazz. It was a Sunday night, the height of the entertainment week, at the Cotton Club in Harlem, the most popular nightclub in the city.

"Ethel took me there because Duke was looking for somebody to sing in his band," recalls Venable. "She was thinking about maybe leaving the revue and she wanted me to get situated with someone else. And she thought I had a better future with Duke than I had with her."

Although many singers and musicians anxiously waited for a chance to join his orchestra, Ellington offered the job to Venable for the rest of the summer. Not only would he sing, but play the trumpet as well. "There were about sixteen men in the band then. I was the fifth trumpet player — the back-up. But I did some singing with the band too. I was a soloist," says Venable.

"I got the job because Duke wanted to help me go to school. But I had to read music. I had to produce because if I didn't, I would have been let out."

"Duke was a disciplinarian. He didn't mind how much fun you had after a performance, but you had to be able to produce," recalls Venable. "He wasn't your father and he didn't set hours."

After their late-night performance — which ended around 2 a.m. — many of the band players would go around to other cabarets and clubs to jam with the musicians there. "Some of the main nightclubs were on 52nd Street, so we would go there and jam till 5 or 6 o'clock in the morning. But these were independent ventures — not band activities. "I would go and so would Barney Bigard and Johnny Hodges. We would go, sit in on the bands and jam — nothing formal."

Both Bigard and Hodges were members of Ellington's orchestra. The former played the clarinet and the latter, the alto sax. Bigard and Venable formed a close friendship and Bigard later helped Venable make a decision ultimately affecting his career.

"The people, the neon lights and the flashy uniforms cast a spell on Venable, and the jazz mesmerized him. "In those days, musicians were in a different world. "We had five or six uniforms — tuxes and tails for the evening, nice business suits for the afternoon. As soon as you finished the performance, the valet would take your uniform because you wore ordinary clothes out on the street. And that was part of the game. People in the audience had to feel that you weren't the same as they were. For good or bad, you were different."

Although the orchestra stayed mainly within the city limits, they did travel occasionally. Ellington's orchestra was one of the few black bands that always traveled first-class, using trains and cars. "We traveled in trains and that was first class," recalls Venable. "Very few bands flew like they do now — most traveled in automobiles or buses."

Venable became smitten with the glamour of his new life and began to reconsider his long held dream — medicine. "I wondered," he says, "when would I ever again be able to perform with a professional band that received top billing? I was going to give up medicine!"

When Ellington heard of this, he encouraged Venable to stay with medicine. "He told me not to get all enamored with this music because it will be here," recalls Venable. "But this was hard for me to accept. It was difficult."

"I was making about $250 a week; in Detroit I had made about $25 to $30 a week. Of course, my main problem was that medical school was so ex-
pensive that I didn't see how I could stay. But then Duke said that as long as I was in medical school, I had a job with his band in the summer so I could make some money.

"Duke also said 'Do something in which your life depends upon your integrity. And if you work hard and study, you'll go up. In music, it isn't that way because you've got to depend upon other guys. When the man signs a contract, he signs it for all the members of the band. And if those guys don't show, the contract is void.' That happened a lot of times in Detroit when I was working little gigs on the weekend."

Bigard also encouraged Venable to return to school. "He said that I should stay in school because I'd probably never get another opportunity, and that being a doctor is more substantial than being a musician," recalls Venable. "Barney was very honest. He didn't color things; he told it like it was."

Despite the encouragement to enter medical school, Venable was not altogether convinced. "I started looking at the bad sides. What if I don't make it at school? Supposing I flunk out? Had I then also lost this chance to go with the world's greatest jazz bands? So I told Duke I had to think about it."

Venable thought about what Ellington and Bigard had said. As a result, he decided to go to school. "When Duke told me I had a job with him every summer regardless of my medical school standing, I had it made."

Venable went back to Wayne State in late September as a medical student and he still "gigged around town on weekends to make a little extra money" because the money he earned each summer was earmarked for tuition.

In 1940, Venable was graduated from Wayne State with a medical degree. He interned and served his residency at Homer G. Philips Hospital in St. Louis. In 1943, he received his Master of Science degree in Ophthalmology from New York University. Venable has been an instructor in ophthalmology at Washington University since 1959, and as assistant clinical professor in ophthalmology here since 1972.

During that time, he continued his interest in music, performing at his church, at private parties including friends' wedding receptions, and currently with a group of other physicians who are also musicians.

Venable really didn't decide between music and medicine in that summer of '35. He just found a way he could combine the two harmoniously. 


d
"You're getting older; arthritis is just something you'll have to live with. There's really nothing I can do for you except prescribe aspirin." This exchange occurred between a physician and an active, otherwise healthy 68-year-old man suffering from pain in his arms and numbness in his hands. The physician was adamant in his opinion; the patient was adamant in his refusal to accept the judgment that nothing could be done to ease the debilitating pain that was affecting his desire and ability to live an active, useful life.

The man was right; something could be done. He sought another opinion from an arthritis specialist, who recommended carpal tunnel surgery. The surgery, performed by Owen S. Kantor, M.D., clinical assistant professor of medicine, is a fairly common procedure that relieves pressure on the median nerve in the wrist. It alleviated the patient's pain and numbness and made him feel "68 years young rather than 68 years old." Had the surgery not been performed, the muscle mass on the thumb could easily have atrophied.

Unfortunately, not all of the 50 million Americans who suffer from some sort of arthritis are as fortunate. Many simply accept arthritis as inevitable and untreatable and most do not seek help from an arthritis specialist.

Although arthritis is this nation's number one crippling disease and has a 13 billion dollar economic impact on our economy, it has been relatively ignored by the lay and medical public alike.

"This has definitely been true, especially in the past," says Bevra Hahn, M.D., associate professor of medicine. "Until quite recently, there were medical schools that didn't even have a rheumatologist on the faculty. Arthritis is a neglected disease because it just does not excite public interest as cancer or heart disease does. And yet some forms of arthritis can be fatal." Because of this lack of expertise on many medical school faculties, it is not surprising that many cases of arthritis are missed or various available treatments are not discussed with the patient. But now, arthritis centers funded by the National Institutes of Health are addressing these problems.

"The NIH originally established 15 of these centers around the country, but that number has now grown to 24. The WUMS Center was established two years ago," says Hahn, director of the Washington University NIH Arthritis Center. "The establishment of these centers indicates that the disease is now being recognized as a real problem that warrants the expertise of a specialist."

Hahn says much of the credit for this recognition goes to the National Arthritis Foundation, which convinced Congress that there should be more funding for arthritis study. "It was difficult to get funding for arthritis study because this disease doesn't kill as often as cancer or heart disease," Hahn says. "But in terms of the number of people who are affected, the associated disability problems, and the social and economic problems brought on by the disease, it is one of tremendous importance."

Obviously the need for these Centers was real and increasing as rapidly as the number of people afflicted with arthritis. The major goals of the NIH Centers are threefold: education of the medical community, education of the lay community and research.

The WUMS Arthritis Center places a great emphasis on community programs, particularly on making services available to the community and educating the public about the disease. "This is a rather unusual direction for the NIH to take," Hahn says. "But they recognize the importance of community awareness and are encouraging the centers to take on this responsibility."

This responsibility to the community has taken the form of educational programs organized by a community relations staff. "All physicians connected with the Center work with the Arthritis Foundation and the Lupus Foundation, and both of these local chapters have outreach programs," Hahn says. "Both organizations conduct public awareness seminars, and our physicians speak to community groups or join panel discussions, answering questions about the disease. The Arthritis Foundation also sponsors a Sunday morning radio program in which we participate. I really believe our efforts are resulting in a more well-informed community."

In addition to educating the lay community, the Center also has made a major effort to educate the medical community about new developments in and treatment for, arthritis. "We don't want a doctor in this area to be unable to recognize carpal tunnel syndrome, for example," Hahn says. "We want to educate every student in medicine, nursing, physical therapy and paramedi-
The WUMS Arthritis Center places a great deal of emphasis on both clinical and basic research. Here Hahn uses a pH meter for preparing buffers which are used in her research.

cal training to care for arthritis patients.

Hahn says this desire to educate the professional is an outgrowth of the National Arthritis Act of 1976. "Hearings held all around the country made several things apparent," Hahn says. "One was that physicians in general practice were generally not well enough informed about the care of arthritis patients. The subject was probably not being adequately taught in medical schools. The hearings also indicated that physicians were not giving arthritis patients the time and attention they deserved."

To help educate the medical professional, Hahn says, the WUMS Center made a videotape showing how to take a history and perform a physical on a patient with joint and muscle complaints. To date, this tape has been used at 15 of the 24 arthritis centers. It has also been distributed to 17 other teaching institutions and has been proven to be an effective instructional lecture.

"We're very proud of this tape and pleased with the response it has received," Hahn says. "Though we designed it to teach primarily first- and second-year medical students, it is popular at American Rheumatism Association meetings and among allied health personnel, especially physical therapists. It is also popular among house officers here and at other teaching institutions."

Another important educational tool of the WUMS Arthritis Center has been a continuing medical education (CME) seminar. "We sponsored a CME seminar on arthritis directed entirely to physical and occupational therapists and nurses," Hahn says. "This support staff has the most contact with arthritis patients."
The seminar was well-received, with 200 health professionals from 11 states participating. Hahn says that testing done before and after the seminar indicated that the participants learned a great deal. "We were able to identify those things that they didn’t know about arthritis," she says. As a result of this testing, a curriculum for the Schools of Allied Health was designed which makes up for past deficits in knowledge.

Over the past three years, the Center has also been involved heavily in various research projects.

The NIH support at the Multipurpose Arthritis Center is somewhat different from the usual NIH grant. "Our grant is supporting development and feasibility studies," Hahn says. "This means research that is really at the beginning stages. If the idea is good and shows promise, then the Center is in the position to apply for more funding."

Hahn says the NIH also encourages the Centers to become involved in more than "bench research." "They want our efforts to include community projects, epidemiology and the study of social problems that go along with arthritis."

The Center recently began a major project in which patients with rheumatoid arthritis and lupus are interviewed extensively about all of their problems, not just which joints or muscles hurt. "We ask the patient how the disease has affected marriage, finances, career and interactions with the rest of the family. We want to evaluate the total cost to the total person," Hahn says.

Through these patient surveys, the Center has reached a better understanding of the problems, both physical and emotional, faced by the arthritis patient. "We ask patients what they perceive as their major problems resulting from arthritis — we are learning that it is not the pain but the disability," Hahn says. "In many of these people, their ability to live a normal life is threatened. They become visibly older."

The findings of the WUMS Arthritis Center survey will be presented to a state task force on arthritis commissioned by the Governor, and used as a basis for state legislation to alleviate socioeconomic problems the arthritis patient faces. "The state cannot be involved in research, but it can provide transportation for people who can’t get to the clinic for treatment," Hahn says.

Some forms of arthritis are age-related, so research becomes even more important because the over 65 population is growing rapidly. "The social and economic implications of this are obvious," Hahn says. "The osteoarthritis that affects 97 percent of the people over 60 slowly worsens over a long period of time. "Although we’re a long way from being able to prevent the disease, there are many forms of treatment available which the average practitioner might not be aware of."

Hahn says it is particularly discouraging to treat a patient who should have had surgery five or six years earlier but who is now bedridden. Many advances have been made in the surgical treatment for arthritis, particularly joint replacements. "Good joint replacements have been available for 15 years and the technique is constantly being refined," Hahn says. "The total knee replacement was developed about ten years ago, and more recently
Hahn uses an analytic balance to prepare agents for her research in systemic lupus.

Another major advance in arthritis treatment has been the development of new drugs. Most important in the treatment of rheumatoid arthritis has been d-penicillamine. Immuran and cytotoxic have proved beneficial for the treatment of very severe forms.

"In addition to these drugs, research has given us a whole array of aspirin substitutes which are more gentle on the stomach," Hahn says. "This has been beneficial to the many arthritis patients who can't tolerate aspirin."

Research in genetics is also playing an important role in discovering who will get the disease and why. "Researchers have learned that there are inherited markers on blood cells which indicate susceptibility to certain forms of arthritis," Hahn says. "One of these, called B27, indicates a 20 percent chance of developing spondylitis, which is arthritis in the back or spine."

Another genetic marker on the white blood cells, called DW4, identifies people at risk for developing rheumatoid arthritis. "These genetic findings are really exciting," Hahn says. "We are getting closer and closer to the hereditary factors that predispose people to this whole set of diseases."

Researchers have also identified certain hormone factors which play a role in a person's susceptibility to systemic lupus. Lupus appears to be a predominantly female disease. "We have increasing evidence that sex hormones are important in protecting men from this disease," Hahn says. "Understanding this relationship between hormones and lupus will offer some answers as to why people get this disease, and will also aid in treatment possibilities."

Women also seem to be more prone to bone softening problems. Bevra Hahn and her husband, Theodore Hahn, Jr., M.D., assistant professor of medicine, are currently doing research in this area. "We are exploring this problem in great depth and surveying many patients seen by rheumatologists for bone softening," Hahn says. "There are a number of different causes of bone softening, but the major ones are aging, being caucasian and being a small-boned woman. A small-boned woman does not have as much bone to lose, and when she does begin to lose it, her bones are much more likely to fracture. We now know that a large, black male is at little risk for bone softening. A tiny, white woman in menopause is at great risk."

The WUMS Arthritis Center is also involved in highly technical research on a subcellular level. Arthritis is not a simple disease. There are more than 100 different forms; its treatment demands the skills of a specialist. But in too many instances, the arthritis patient is not referred to a specialist.

"The many different varieties of the disease are diagnosed through an appropriate history, physical blood tests and x-rays," Hahn says. "But, with so many varieties, the physician has to know what he's looking for. It's simply impossible for a person outside of the field to have all of that expertise, but we would hope he would know when a case is out of his realm of knowledge. Otherwise, the arthritis patient may be suffering needlessly."

Fortunately, more and more physicians in the area are referring their arthritis patients to the WUMS Center. "Hundreds of patients are admitted to the Center every year," Hahn says. "and any physician who admits a patient here is expected to make that patient available for teaching purposes. Unfortunately, by the time many of the patients arrive, they are in pretty bad shape."

Nevertheless, a great deal can be done for these people. Hahn says it is extremely rewarding to treat people who can obviously benefit from the many therapies available, and to see their quality of life dramatically improved.

"In all but the most severe cases, we can rehabilitate a patient," she says. "We can usually prevent a condition from worsening, and we can always sympathize. Although all chronic arthritics have to accept some degree of discomfort and disability, 96 percent may benefit from rehabilitative and therapeutic procedures."

"Simply to pat someone on the back, hand him two aspirin and say 'you'll have to learn to live with the pain' is not practicing good medicine. Although we have many sophisticated treatments available, we have a long way to go over the next several years. Many goals have not yet been reached. But, if we can make our current knowledge available to physicians and allied health professionals, I would feel the Center has reached a worthwhile goal."

One out of every ten people has arthritis; it costs Americans $4.7 billion annually in lost wages. We can't afford to ignore it.
Fungal Infection: The New Concern

*Reprinted from Preview, a publication of Eli Lilly and Company.

With systemic and opportunistic mycotic infection on the rise, a unique battle plan against fungal pathogens is being designed by Dr. Gerald Medoff and his colleagues at Washington University School of Medicine.

The School recently received a five-year grant for more than $1.2 million from the National Institutes of Health to establish one of two Mycology Centers in the country.

For generations, starlings had lived in peaceful coexistence with their neighboring flora and fauna in a bucolic area of the southeastern United States. Bats were viewed as harmless fantasy creatures with a certain affinity for witches and vampires and Halloween. Then factories began to spring up in the region, and huge tracts of soil were ripped up in an accelerated process of "instant urbanization."

With the sudden influx of humans, people soon began to experience nonspecific symptoms, such as fever, chills, weight loss, anorexia, night sweats, and respiratory complaints. Medical examination of some of the diseased patients revealed splenomegaly, leukopenia, pulmonary and palatal lesions, and laryngeal erosion. The community had undergone widespread exposure to *H. capsulatum.* Although most of those infected eventually recovered, a number of patients continue to show persistent symptoms of disease. New cases are reported regularly despite intensive preventive efforts by practicing physicians and public health officials.

Similar scenarios are being enacted all over the country and the globe, according to Dr. Gerald Medoff, Chief of Infectious Diseases.

"Fungi are free-living forms found in soil, decaying vegetation, and bird excreta," explains Dr. Medoff. "Because of the rapid urbanization of our society, we are impinging on regions which humans ordinarily would not inhabit. As our cities expand, we are moving into areas where birds and bats have lived for centuries. We are taking over farmland and building garden apartments. We are digging up soil that is contaminated with bird droppings and is a source of histoplasmosis. As we dig up this soil, we aerosolize and inhale it, and inhalation is the primary path of entry for fungal pathogens. It's safe to speculate that systemic mycotic infection will continue to increase and that it is becoming a significant cause of human distress."

Epidemiologic data tend to bear out Dr. Medoff's concern. Reports from major medical centers indicate a steady rise in patients presenting with blastomycosis, histoplasmosis, and coccidioidomycosis. The National Cancer Center finds that cryptococcal meningitis — often afflicting patients with malignancies — is now the chief form of meningeal infection and outstrips the bacterial form of the disease.

In addition to the rise in systemic illness caused by typically pathogenic fungi, medical centers throughout the country are experiencing a parallel increase in "opportunistic" fungal infection. "You can probably get as many definitions of 'opportunistic infection' as there are researchers in infectious disease," comments Dr. Medoff. "I think of opportunistic infection as resulting essentially from decreased host resistance rather than from the virulence of the offending organism. A host with weakened immunologic defenses is fair game for a variety of pathogens, including fungal organisms — *Candida, Aspergillus, Cryptococcus* — that ordinarily would not cause infection in individuals with adequate host response."

Unless immunologic protection has been diminished, notes Dr. Medoff, *Candida albicans* is usually benignly omnipresent in
the environment and is part of the normal flora of the vagina, throat, mouth, and gastrointestinal tract; species of *Aspergillus* are harmlessly ubiquitous in the atmosphere. *Cryptococcus neoformans* seems to be an "intermediate" organism — about 50 percent of patients with cryptococcal meningitis show decreased host response, whereas the remaining 50 percent have no apparent immunologic deficiency.

Ironically, the growing problem of opportunistic fungal infection is largely a consequence of medical progress. Because powerful immunosuppressives are now routinely administered to transplant patients and to those with malignancies, hospitals are currently filled with an immunologically compromised population. Long-term catheterization, a characteristic of many sophisticated surgical techniques, has opened new portals of entry for contaminating fungi.

"Added to this iatrogenic picture is the liberal employment of antibiotics that predisposes patients to fungal disease," declares Dr. Medoff. "Broad-spectrum antibiotics, such as tetracycline or penicillin, assault the normal bacterial flora as well as the specific pathogen; this flora is one of our chief defenses against infective organisms. It has been clearly established, for example, that overuse of tetracycline — an oral drug that is commonly prescribed because of its broad spectrum — can damage the normal flora and predispose the patient to a variety of candidal infections."

Despite such evidence that signals the evergrowing menace of fungal infestation, Dr. Medoff finds that many physicians cannot conceive of mycotic infection in terms of serious disease. He observes:

"Practitioners still tend to equate fungal infection with athlete's foot or some equally trivial condition. Actually, the systemic forms of fungal infection are often insidious and progressive processes that eventually result in debilitating sequelae and even death, especially if they have been misdiagnosed or mistreated. Moreover, fungi are very 'tough customers.' They possess a cell wall and membrane that are difficult to penetrate with chemotherapy. They are more complicated than bacteria, and in some ways they are more complicated than viruses.

"Unlike viruses, which must exist within human cells, fungi can exist by themselves; they are self-sufficient organisms. The systemic fungi go through a very elaborate two-phase process of adaptation — yeast and mycelial — which has yet to be clearly delineated. It is interesting to note that the frankly pathogenic fungi are capable of this dimorphic process, whereas those that are opportunistic agents are not. Furthermore, they are so morphologically similar to animal cells that any measures taken to control the fungi often affect the host cells as well. We know there is no such thing as a completely sterile environment — if you eliminate one flora, another will take its place. Thus, if we develop antibiotics sufficient to deal with every bacteria, we are probably going to be overrun with fungi. It's as if this other invader has just been lurking, waiting for its chance. And now it appears that the time of the fungus may be imminent."

The AmB Group

Dr. Medoff did not become intensively involved in antifungal research until his appointment at the Washington University School of Medicine in St. Louis. Having been affiliated with the Massachusetts General Hospital in Boston, a region where systemic fungal disease is relatively less frequent, he was intrigued by the sizable number of patients from the St. Louis area who had histoplasmosis and cryptococcal meningitis. Concerned that the treatment available was limited, he began to investigate methods of improving antifungal therapeutics.

Soon Dr. Medoff was voicing his concern to Dr. George S. Kobayashi, a mycologist in the division of dermatology and associate director of Barnes Hospital's Diagnostic Bacteriology Laboratory. The two researchers began to design a series of experiments in which pathogenic fungi were challenged by antibiotic combinations. After the initial experiments were launched, Dr. Kobayashi described early results to Dr. David Schlesinger, Professor of Microbiology. Dr. Schlesinger immediately became an enthusiastic member of the team; while studying fungi with defective cell walls, he had observed similar sensitivity patterns to a variety of antibiotics.

Inevitably, the Washington University investigators focused their efforts on amphotericin B (amb), a polyene antibiotic that has been the chief systemic antifungal agent for almost two decades.

"In treating systemic fungal infections," Dr. Medoff points out, "we have been at the stage where antibacterial chemotherapy was twenty-five years ago, right after the discovery of penicillin. Essentially, we have been limited to only this one antifungal agent. AmB is effective because it penetrates the fungal-cell membrane and binds to ergosterol, which is the principal sterol in mycotic cells. After binding, it increases membrane permeability and eventually lyses the cell. Unfortunately, amB's affinity for ergosterol is not specific — it also binds pretty well with cholesterol, the principal sterol in animal and human cells; hence, it always carries a potential for cytotoxicity. Employed against systemic fungal disease, amb must be administered intravenously in fairly large doses over long periods of time; it can be as toxic to the host as to the organism."

Continuing his reference to antibacterials, Dr. Medoff notes that chemotherapeutic efficacy against specific bacteria often has been improved by the synergistic action of two agents; he cites the combined use of penicillin and streptomycin against enterococci as a particularly dramatic example of such synergy. In other instances, antibacterial drug treatment has been enhanced by the concomitant use of agents, such as ethylenediaminetetraacetate (EDTA), which penetrate the bacterial cytoplasmic membrane.

Could amb combine with other antifungal agents to diminish toxicity while maintaining or enhancing efficacy? Could amb potentiate the antifungal properties of antibiotics which have not been usefully employed in mycotic infection because of poor penetration, particularly those that inhibit RNA or protein synthesis?

As Drs. Medoff, Kobayashi, and Schlesinger set about to answer these questions, they found that amb — in addition to its usefulness in antifungal treatment — also apparently potentiates antitumor agents and stimulates immune mechanisms. The amb research group at Barnes Hospital has now expanded to include a clinical oncologist, an immunopathologist, a pediatrician, two immunologists, two cell biologists, and a mouse geneticist, as well as five or six additional antifungal researchers. The group meets
each Friday at 7:30 a.m. over coffee and doughnuts to discuss ongoing projects and share research observations.

"I don't know of any other group at our own institution that cuts across so many disciplines, and I doubt that there are many such groups at other medical centers," says Dr. Medoff. "All of us have our own research interests aside from amB, but we share this one common interest and we all participate. It really has been a marvelous thing. We bring together different disciplines and experiences, and the give-and-take often stimulates a fresh view of our own research preoccupations."

Whatever the specific research area, this multidisciplined fascination with amB stems from its unique ability to "punch holes" in cell membranes — much as a football lineman clears the way for the ballcarrier.

AmB and 5FC

Introduced clinically several years ago, 5-fluorocytosine (5FC), a fluoropyrimidine, has never fulfilled its initial antifungal promise. Although it has some effectiveness against a variety of yeasts — mainly by inhibiting nucleic acid synthesis via its effect on the pyrimidine biosynthetic pathway — it has become increasingly evident that many yeast strains are resistant to 5FC. Experimental studies and assays of cultures taken from patients treated with 5FC indicate that this resistance stems from the failure of the pyrimidine analog to penetrate the yeast.

It was this latter observation that impelled Drs. Medoff and Kobayashi to launch a series of investigations in which the capabilities of amB to increase permeability would be utilized to enhance the uptake of 5FC and, eventually, other agents. "The rationale behind these studies," says Dr. Medoff, "has two aims": (1) to lower the dosage levels of amB, thereby decreasing the toxic potential frequently associated with this agent; and (2) to permit the second agent to be preferentially taken up by the fungus but not by the host. The success of this line of inquiry is underscored by the fact that a number of medical centers have now initiated clinical trials with the amB/5FC combination.

Prior to in-vitro testing of the two agents in combination, the Washington University researchers employed amB and 5FC singly against Saccharomyces cerevisiae, C. neoformans, C. albicans, and C. tropicalis. They also worked out the minimum inhibitory concentration (MIC) of each agent — the lowest concentration of drug that completely suppresses fungal multiplication.

In most cases, the MIC of 5FC was in excess of 200 mcg./ml., and this agent was only partially fungistatic even at this level. MIC’s of amB were also only partially inhibitory to the growth of the yeasts and never produced a killing effect. Even when the MIC’s of each agent were doubled, growth inhibition was only slightly potentiated.

These unimpressive results were strikingly reversed when amB and 5FC were combined against the same organisms in concentrations of less than one half the individual MIC of each agent. Among the key observations to emerge from these in-vitro experiments:

- The amB/5FC combination is apparently synergistic at concentrations that produce little or no effect when the drugs are employed alone.
- At certain synergistic concentrations, amB/5FC results in a marked killing effect.
- Fungicidal response to the combination is ten or more times greater than the killing effect of the agents used alone.
- The combination is apparently completely fungicidal against S. cerevisiae.

Further documentation of amB/5FC synergy has come from animal studies conducted by the Washington University investigators. When employed against A. fumigatus infection in mice, the amB/5FC combination is considerably more effective — at clinically achievable blood levels — than single-drug therapy. Researchers at other medical centers report similarly promising results when the combination is used in vivo against Cryptococcus and C. albicans.

Currently, Dr. Medoff and his colleagues are participating (along with ten other medical centers) in a fungus study group that is evaluating the effectiveness of amB/5FC against clinical cryptococcal meningitis. Patients accepted for the study are asked to consent to random assignment in either of two groups. One group receives the traditional single dose of amB, an equivalent number of patients with cryptococcal meningitis receive half the standard dose of amB plus half the clinical dose of 5FC. Both groups are followed intensively for a year, with careful monitoring of pertinent clinical and laboratory parameters.
"Preliminary data suggest that the final results are going to be quite positive," reports Dr. Medoff. "Our primary goal has been to find a chemotherapeutic approach that would maintain the effectiveness but reduce the toxicity of the traditional amB regimen; now it looks as if we’re going to get enhanced effectiveness against cryptococcal meningitis as well as decreased toxicity. If these favorable data hold up when the results of the full clinical trials are completely evaluated — and if unexpected negative effects are not observed — the first effective antifungal drug combination may be available to practitioners in the not-too-distant future."

**AmB and Rifampicin**

Clinically efficacious as an antibacterial primarily because of its apparent specificity for bacterial RNA polymerase, rifampicin has never shown a similar tendency to inhibit RNA synthesis in yeast cells. An ongoing amB/rifampicin study at the Washington University School of Medicine now suggests that rifampicin’s known antiviral properties can be potentiated against fungi via enhanced intracellular uptake. Results developing now may have important clinical ramifications.

In laboratory experiments similar to those carried out for 5FC, Dr. Medoff and his colleagues have challenged S. cerevisiae and H. capsulatum with rifampicin at concentrations as high as 100 mcg/ml. As with 5FC, the use of rifampicin alone yields virtually no antifungal benefits. However, when rifampicin is combined with amB at doses well below the respective MIC’s of each agent, the resultant penetration of rifampicin into the yeast cell permits significant fungistasis and blockage of RNA polymerase function. These provocative findings are being substantiated in studies of mice infected with A. fumigatus, H. capsulatum, and Blastomyces dermatitidis. Dr. Medoff reports that rifampicin used alone at doses of 50 or 100 mcg has no beneficial effect against murine aspergillosis and, in certain instances, actually appears to intensify infection when compared with controls. By contrast, 50 or 100 mcg of rifampicin combined with 10 mcg of amB — a dosage far below optimum levels — is markedly effective against experimental aspergillosis.

"Survival rates of the combination-treatment group are considerably higher than those of either the single-drug or untreated groups," continues Dr. Medoff. "Since rifampicin alone has no therapeutic value and amB at a dose of 10 mcg is only marginally active, the in-vivo interaction of these two drugs would appear to be synergistic."

Despite the enhanced effectiveness of combination therapy, mycologic cultures taken from sacrificed mice indicate that the amB/rifampicin regimen does not completely eradicate *Aspergillus*. Whereas aspergillus generally cannot be cultured from the brains, lungs, spleens, or livers of mice receiving combination treatment, approximately one-third of this group continues to show culture-positive kidneys. Macroscopically, these kidneys appear hydropic, with large pelvic abscesses.

"Actually," Dr. Medoff points out, "these results are still impressive when compared with those of single-treatment or untreated groups. On histopathologic examination of the combination-treatment groups, mycelia are seen in the renal pelvises in the form of fungus balls but without apparent invasion of pelvic tissue. In contrast, untreated animals dying of *Aspergillus* infection show invasive disease of brain, lung, and kidney.

Speculating on the combined regimen’s failure to eradicate aspergillus in the kidney, Dr. Medoff suggests that local renal conditions — such as depressed phagocytic cells or inactivation of complement — may underlie the persistence of infection. He is hopeful that "mycologic sterility in the kidneys can be achieved via dosage adjustments, probably by employment of higher doses of amB."

Results of the amB/rifampicin combination against murine histoplasmosis and blastomycosis are virtually identical. Rifampicin alone shows no therapeutic value against either of the causative organisms at dosages up to 100 mcg, whereas a regimen of 50 or 100 mcg of rifampicin (or as little as 25 mcg against *B. dermatitidis*) plus 10 mcg amB controls infection and prolongs survival. Moreover, enhanced efficacy is apparently not accompanied by increased toxicity.

These findings "have obvious clinical significance," stresses Dr. Medoff. "They indicate the very real possibility of adding another effective drug to our sparse array of available antifungal agents. Although one cannot easily extrapolate results from animals to humans, favorable in-vivo data suggest that it is certainly worthwhile to study the efficacy of this combination in human antifungal infections, particularly those that have been unresponsive to amB. As a matter of fact, one of our chief priorities is the institution of such clinical trials with the amB/rifampicin combination."

**Additional AmB Studies**

Encouraged by the data emerging from clinical trials with 5FC and the in-vivo results with rifampicin, Dr. Medoff is nonetheless convinced that additional basic research is necessary to exploit amB’s antifungal potential fully. Several lines of investigation are currently being pursued by the Washington University researchers:

- **Actinomycin D**, *mycophenolic acid glucuronide*, and *tetacycline*. In addition to substantiating amB’s permeating and potentiating abilities further, laboratory experiments using amB in combination with these three antibiotics are providing other provocative data. One interesting observation, for example, is that the mycelial phase of dimorphic fungi is apparently more sensitive to amB, whereas the yeast phase appears to be more susceptible to actinomycin D. This observation may eventually be important in assuring proper antifungal employment of amB and/or actinomycin D; it may also be useful in studies delineating the transition of dimorphic fungi from one phase to the other.

- **Filipin**. This research avenue is furnishing additional proof that the toxicity and effectiveness of polyene antibiotics are determined by the drug’s relative propensity to bind to the predominant sterol in cell membranes. As with many polyenes, filipin’s toxicity at the present time precludes its clinical use. When *S. cerevisiae* yeast cells and human red blood cells are challenged separately by filipin and amB, the toxic/therapeutic ratio of these two polyenes is clarified by the following observations: (1) Filipin is more potent in lysing human red blood cells, whereas amB is more potent in inhibiting yeast cell growth; (2) the effects of filipin are more efficiently inhibited by added cholesterol, the major membrane sterol in human-cell membranes.
whereas the effects of amB are more efficiently inhibited by ergosterol, the major sterol in yeast membranes.

"The simplest interpretation of these results," adds Dr. Medoff, "is that amB/ergosterol interactions are stronger than those of amB and cholesterol and that filipin/cholesterol interactions are stronger than those of filipin and ergosterol. In the clinical situation, two types of cells are treated with polyene antibiotics — the fungus and host cells. Thus, to understand the relative toxicities of different polynexes and their basis in molecular interactions, at least two relevant cell types and two polynexes of different toxicities must be studied and compared. Our findings show that when this is done, an over-all rationalization of relative toxicities and binding affinities becomes clear."

**AmB Binding.** Utilizing an assay based on enhanced fluorescence of amB in acid solutions, the Washington University investigators have delineated two types of amB binding: (1) A weak reversible binding that occurs at temperatures as low as 0°C., even in the presence of inhibitors of energy metabolism; and (2) a strong irreversible binding that depends on considerably higher temperatures and adequate energy metabolism. Our strong binding is correlated with yeast cell killing. Weak binding probably involves only the outer layer of the cell membrane, whereas strong binding apparently requires disruption of hydrophobic regions of the membrane.

**Polymyxin B and Tetracycline**

While continuing to study amB in combination with various other agents, Dr. Medoff and his colleagues are expanding the scope of their investigations to include non-amB antibiotic combinations. In-vitro experiments with tetracycline and polymyxin B suggest that this approach may have fruitful possibilities.

Seldom used clinically because of its toxic hazards, polymyxin B alters cell permeability by binding to the negatively charged phospholipid component of the membrane. Tetracycline has been shown to inhibit protein synthesis in yeast extracts but has been ineffective against whole organisms.

**Could polymyxin B be utilized to 'punch holes' in yeast cell membranes — much in the manner of amB — and potentiate the antifungal effects of tetracycline?**

The Washington University researchers report that tetracycline, tested singly against C. albicans and S. cerevisiae, has no effect on the two organisms at concentrations as high as 500 mcg./ml. Polymyxin B is capable of inhibiting both RNA and protein synthesis but only at relatively high concentrations above the MIC.

The picture changes dramatically when polymyxin B and tetracycline are used in combination. At low concentrations, which result in little or no antifungal activity when the agents are employed singly, the polymyxin B/tetracycline combination effectively inhibits protein synthesis and kills 99 percent of C. albicans and S. cerevisiae colonies.

Dr. Medoff adds: "An interesting observation emerging from this study is that potentiation of tetracycline occurs only when the yeasts are first incubated overnight in the polymyxin B alone. When the two antibiotics are added simultaneously — or when tetracycline is introduced first — the antifungal effects of polymyxin B are reversed by
tetracycline. This apparent antagonism is probably related to the ionic properties of polymyxin B, which has been shown to interact with many acidic substances. When tetracycline, a fairly acidic substance, is introduced first or simultaneously, it interacts with polymyxin B at the cell membrane and restrains penetration. When the yeasts are pretreated with polymyxin B, permeability is already achieved before the tetracycline is introduced. Consequently, the tetracycline also can penetrate.

"Even though the concentrations of the polymyxin B/tetracycline combination are much lower than those of the antifungals used singly, they are probably still too high to risk clinical application. However, these studies suggest that alteration of cell permeability to achieve synergy can be attained with agents other than amphotericin B. To my mind, this insight is more important than the specific findings: we have barely scratched the surface in elucidating the antifungal properties of agents already in our armamentarium."

"Footprints" of Fungi

Accurate diagnosis of suspected fungal infection is often tricky and time-consuming. Specific antibodies or increases in antibody titers may not appear for several weeks, and many hosts are incapable of producing adequate antibody responses. Serologic detection frequently requires special diagnostic techniques that the average bacteriologic laboratory is not equipped to perform. Added to these problems is the fact that cultures of fungi are notoriously slow-growing and difficult to maintain.

In an effort to speed up and possibly enhance mycotic diagnosis, Dr. Medoff and his co-workers, Dr. Harvey Liebhaber, Dr. J. Russel Little, and Dr. G. Kobayashi, have just launched an intensive search for the "footprints" of fungi — end products and/or antigens that can be rapidly identified and correlated with specific fungal pathogens. This medical sleuthing project is still in the very early stages of animal experimentation; the Washington University researchers are currently preparing reagents and attempting to isolate possible antigens from blood and spinal fluid. If successful, such experiments could lead to the development of a rapid method of screening fungal infection candidates.

In the meantime, Dr. Medoff emphasizes that most fungal infections will continue to be managed by the practicing physician. "Probably the most direct and effective way of improving management of mycotic disease is simply to increase our index of suspicion. I would expect, for example, that physicians in the Ohio and Mississippi river valleys are adequately suspicious of histoplasmosis, that practitioners in the South are looking out for blastomycosis, and that those in the desert areas are considering coccidioidomycosis. In addition, physicians must become sufficiently aware of the correlation between opportunistic fungal infection and the overuse of antibiotics, sophisticated surgical procedures, and immunosuppressive chemotherapy.

"Improved diagnosis and treatment must be accompanied by careful epidemiologic studies. Despite the apparent increased incidence of fungal disease, epidemiologic monitoring is actually decreasing. The recent elimination of the Fungus Station in Kansas City — which, for a number of years, had been keeping track of fungal infections — is most unfortunate, as are the cutbacks in mycology training programs. There may be a delay of some years before the medical community and government health agencies wake up and say: 'Hey, we have no mycologists!' We will have lost much valuable time by not controlling this increasingly prevalent and formidable invader."

About the researcher:

Dr. Medoff is Professor of Medicine, Washington University School of Medicine, and Chief of the Division of Infectious Diseases at Barnes Hospital, St. Louis. He was born November 9, 1936, in Brooklyn, New York, and received his M.D. from the Washington University School of Medicine in 1962. Dr. Medoff is a member of the American Mycological Society, American Association for the Advancement of Science, American Society for Microbiology, American Federation for Clinical Research, American Society for Clinical Investigation, and the Infectious Diseases Society of America.
For CIBA Award-Winner, “Community Service” Is Everyday Life

By Mary Poluski

Mark Manary is a second-year medical student who lives in a turn-of-the-century house in the Central West End of St. Louis—an area which, years ago, was fashionable and housed the city’s elite along cloistered streets. But the elite are gone and their houses are now inhabited by a new breed—urban homesteaders. These new homesteaders are young, strong-willed and committed to stabilizing the area and even to revitalizing it. Manary is among their ranks.

Manary is active in a non-profit corporation working to stabilize his community. He is instrumental in such projects as a children’s carnival and a neighborhood recycling depot. Classmates describe him as embodying the essence of community service—a trait recognized by a 1979 CIBA Community Service Award.

Sophomore students at various schools of medicine receive this award from the CIBA Pharmaceutical Company for outstanding extra-curricular activity within their communities. The award includes a complete Netter Atlas Encyclopedia for each recipient.

Recipients are selected by their classmates either in a general election, or by a committee of students. Manary was unanimously selected by a committee of five students from his class. “The award is supposed to be for extra-curricular community service, but so much of Mark’s daily world revolves around the community,” says Paul Organ, class president and member of the committee. “We were impressed that he devotes so much effort and time to his community and still maintains his student standing.” To Manary, his community activities are not outside interests—they are an important part of his life.

Manary is from Midland, Michigan. “At home,” he says, “we don’t see poverty. We only read about the American urban problem in Time Magazine.” Today, he lives amid such problems in a three-story, 18-room house with 11 other people, including a family of six. He refers to this group as “the household.” As its business manager, he is responsible for collecting rent and allocating money for living expenses, food, heating and minor repairs. “The household has taught me how to live with other people, how to exercise leadership, how to organize a task,” says Manary.

“The household is a group of people who are interested in living in a Christian community. A few of the people come from broken situations—not alcoholism or drug abuse—but they may be recovering from a depression or moving from an orphanage. These are people who are not yet ready to live by themselves,” he says.

Manary received the 1979 CIBA Community Service Award at Washington University School of Medicine for his daily assistance in neighborhood revitalization and stabilization, and personal assistance to people in the area.

Manary is also a member of Cornerstone Corporation, a neighborhood organization designed to maintain economic diversity within the community. “The neighborhood is in a period of transition. There are some abandoned buildings, and property is changing hands. The rich are moving in, and the poor are having to move out.” To prevent an uneven distribution of wealth and to maintain diversity, the corporation was formed. “The corporation owns apartment buildings in the area and rents to low-income families. I’ve worked with the tenant relations committee, and we deal with failures to pay rent, problems of noise or destruction of property.

He is also an occasional plumber, painter and wallpaper hanger, and lends a hand on maintenance projects for the corporation. Through his work with Cornerstone Corporation and his daily life at the household, Manary comes into direct contact with people who have the kind of urban background that he formerly only read about. These situations have given him insight into urban problems, including medical problems that the poor encounter because many do not know where to go for a medical problem. These problems are ignored until they become critical—emergency-room cases,” he says. “Often, there is no preventive medicine—just neglect.”
Three years ago, Washington University Medical School, with funding from the Sunnen Foundation in St. Louis, began an innovative seminar which challenges students to relate medical technology to the economics, ethics and cultural values involved in population growth and regulation.

The seminars were initiated and organized by Hugh Chaplin, Jr., M.D., an immunohematologist who is professor of medicine and the William B. Kountz Professor of Preventive Medicine. With a grant from the Rockefeller Foundation in 1972, Chaplin surveyed 110 medical schools in the U.S. and Canada. His questionnaire was designed to determine the amount of time in the schools’ curricula devoted to issues in population regulation, and to elicit opinions of faculty members about physicians’ roles in public policy and in patient care related to population regulation and fertility.

“Population growth impacts community health in its broadest sense, and affects nearly every aspect of the quality of life,” Chaplin said. “For example, paving over farmland for highways and suburban housing and malls makes less land available to produce food for the increasing number of people whose existence made it feasible to develop the new housing and roads.” The size and ages of the populations of countries influence the needs and capabilities of those countries and their governments’ decisions about foreign trade, foreign policy, and the health and welfare of their people.

Chaplin’s interest in population and world health was piqued in 1971 when, he said, “population was a hot topic in the United Nations, the Nixon administration and, consequently, the media.”
With a heightened awareness of population issues, Chaplin decided to survey medical schools to learn about the extent of, and plans for, education in the nonmedical aspects of population growth and control. To Chaplin, it seemed important that physicians be prepared to give informed responses not only to patients, but also to public questions arising from advances in scientific technology of fertility regulation. “This is an era of increased sexual freedom and expanded public candor in talking about human sexuality and individual freedoms, and an age of growing concern about dwindling resources,” Chaplin said.

The questionnaire results indicated that population issues were not covered in medical school curricula. Faculty members were interested, however, and more than 93 percent of the recipients responded to the survey. More than 90 percent of the respondents indicated that medical school freshmen were inadequately informed about contraception, population dynamics, and the ethical, legal and psychosocial aspects of population regulation. However, most of the schools devoted less than half an hour to studies of the attitudes of economists, industrialists and the public about population stabilization programs.

Fertility regulation topics more closely focused on the doctor/patient relationship, such as the medical and ethical aspects of sterilization and abortion procedures and decisions, were rated as very important by a majority of the respondents and were usually given an hour or more in curricula.

Chaplin followed his survey with a successful application to the Rockefeller Foundation for a grant for a three-year experimen-
Select Committee on Population

University of Wisconsin sociology professor Dr. Larry Bumpass, who has worked with the U.S. Fertility Survey, will conduct the seminar on sociologic-behavioral aspects of fertility control.

"This year," Chaplin said, "Dr. Ved Sharma of the economics department of Mankato State University in Minnesota, will be with us in place of our own Dr. Harold Barnett, who is on sabbatical. He recommended Dr. Sharma, who is from Calcutta."

Dr. Georg Borgstrom, professor of food science and geography at Michigan State University in East Lansing, will speak on world food supplies and population growth. Dr. Allen O. Miller, director of postgraduate studies and professor of systematic theology and philosophy at Eden Theological Seminary in St. Louis, will lead the seminar on ethical aspects of population stabilization.

Chaplin organizes the seminars and selects the speakers, and his office arranges travel and accommodations. Chaplin described his role at each session as "the emcee, introducing the speaker, umpiring the question-and-answer period, and making sure that the more articulate and keyed-up students don't dominate and discourage some of the more quiet individuals."

Informality is the style, with the sessions held in the Shaffer conference room around a large table. After the speaker's 50-minute presentation, there is a break for soda or beer and pizza. The final hour is devoted to questions and answers.

The desire for informality and vigorous discussion restricts attendance to 30 students. "If it became too big, we would lose something that is important to the students." Chaplin selects the participants, giving priority to seniors, to any student previously turned down, and to achieving "a good mix." He explained, "The discussions work best when there is a variety — ethnic variety, married and unmarried, a range of academic ranking, and a proportionate number of women students." Students who apply are not just those going into Ob/Gyn. Some have expressed intentions of working in a developing country for a time. The seminar is especially important to them.

The discussion among students and speakers is what makes the issues real and relevant. Chaplin has videotaped recorded past seminars and surveyed student opinion of the taped and the live session. "The students definitely preferred the live sessions," Chaplin said. "We asked if they would watch the tapes if they would be made available, and the response was a resounding No."

After three years as part of the curriculum, the population seminars continue to gain popularity, although Chaplin had expected student interest to wane with media coverage. Perhaps the oil shortages of the past few years have heightened awareness of the problems of more people diminishing finite resources. "Fertility," said Chaplin, "is such an important aspect of health-related legislation and regulations. Actual implementation of fertility regulations on a large scale is more a political decision and a sociological issue than a medical issue. But the scientific research underlying the ability to make those decisions is almost all done by medical research groups, and the techniques of enhancing or restricting fertility are carried out by physicians."

Chaplin believes that it is important to prepare physicians to respond to their patients' and their communities' questions about the technical, practical and ethical issues in fertility.

"Physicians should not beg the question by saying 'that's not my field.' Physicians can be more involved in policy decisions, and can better serve patients if they have a broad awareness and knowledge."

Students here seem to share his attitude, as evidenced by the growing numbers who apply for the elective seminar. "We're getting good reviews on the grapevine."
100 Million
38% more ♀
15-35 yr age
Honoring Dr. Harford

Carl G. Harford, M.D., professor emeritus of medicine and former chief of the Division of Infectious Diseases, was graduated from the School of Medicine in 1933 and has spent the past 42 years on the full-time faculty. Three years ago, the Annual Carl Gayler Harford Visiting Professorship of Infectious Diseases Lecture was established to pay tribute to Harford's many contributions to the University and to his excellence as a physician.
This year's Visiting Professorship took on added importance with a reception and the unveiling of a formal portrait of Harford in addition to the annual lecture. The lecture was given this year by George G. Jackson, M.D., (left behind Harford), professor of medicine at the University of Illinois College of Medicine. At right is Gerald Medoff, M.D., professor of medicine and chief of the Division of Infectious Diseases.
Honoring Dr. Harford

Mildred Trotter, Ph.D., professor emeritus of the Department of Anatomy and Neurobiology; J. Russell Little, Jr., M.D., professor of medicine and director of infectious diseases at The Jewish Hospital of St. Louis were among those honoring Dr. Harford.

Harford and his wife, Mary, were joined by family, friends, colleagues and students at a reception in the penthouse of Olin Hall. They came to honor a man who has become an integral part of Washington University.
Dear Fellow Alumnus:

I suppose the Medical Center must be considered to be young in heart, since it continues to show signs of healthy growth. The addition of the West Pavilion between the East Pavilion and the Queeny Tower has literally put a new front on the Washington University Medical Center Complex. The changes in the twenty-five years since the Class of '55 graduated have been dramatic. Telescoping that time fragment, a lot of dramatic things have happened to us individually too!

The Alumni Association remains vital and active. The year started with an enthusiastically attended Freshman Welcoming Party at the Vineyard in St. Charles on a delightful September evening. A Welcoming Party was given for new House Staff in November around the Queeny Tower swimming pool.

The Medical Center’s Continuing Education Programs under Elmer B. Brown, M.D., Class of '50, have served our alumni and others with a most interesting variety of excellent symposia. Over 2,000 attend these programs each year.

The 28 members of your Executive Council spent a very interesting evening at the last meeting, in earnest discussion with Gene Bricker, M.D., Class of '34. Gene is a member of the new committee charged with taking a close look at the future of the Medical Center and making recommendations about it. He would welcome input from any of you as well. I am sure.

The annual Student-Teaching awards this year were made to Dr. David Menton in the Department of Anatomy and Dr. James W. Holcroft, formerly in the Department of Surgery. These men are chosen by the students in appreciation for their excellence. Our congratulations to both of them.

Alumni support of the Medical Center reached an all-time high in 1979. Inflation and a cut-back in government-supported programs have made alumni support essential. I would urge you to support not only the Century Clubs, but to join with many others in the Eliot Society. Eliot Society dues are being used to endow professorships within various departments of the Medical Center that do not have these. This is one chance to make major contributions to the Medical Center and know exactly what they are going to be used for, now and in the future.

The Student Alumni Loan Program becomes more and more needed as there is less federal support available, and inflation continues to make life difficult for those trying to attend medical school. In 1979 we made sixty-one loans totalling $25,305.00. Repayments on previous loans are quite healthy, but the expanding need for loans underlines a continuing need for donations to this program.

By the time this letter reaches you, those of us who were both smart and fortunate enough will have attended the annual Alumni Clinical Conference, rejuvenating ourselves in the warm sun on the beach at Ixtapa, Mexico, while listening to an excellent series of lectures given by various professors in the Medical Center. You really should think about going next year!

And don’t forget to make plans for the Class Reunions, May 8-10, 1980. A good program has been planned; the alma mater is well worth visiting again, and your friends look forward to seeing you here.

Robert C. Drews, M.D. ’55
President
Class Notes

'20s

Herbert Anderson, Jr., '26, was honored by the Los Angeles City Council. A plaque inscribed, "1979 Physician of the Year," was presented to Dr. Anderson at a formal dinner at the Friar's Club in Beverly Hills.

Lee M. Hamm, '29, Lincoln, IL, has celebrated 50 years in active medical practice. He was a founder of the Abraham Lincoln Medical Group and was instrumental in developing an intensive care unit at the Abraham Lincoln Memorial Hospital.

'30s

Lewis S. Ent, '31, Cairo, IL, was awarded a gold medal and certificate for his work on Chronaxy. The honors were conferred at a meeting of the International Association of Neurologists in Vienna, Austria.

Edward J. Kloess, '32, Belleville, IL, has retired from private practice, but is doing volunteer work for the Red Cross and Retired Senior Volunteer Program.

Robert S. Smith, '33, is an honorary member of the Idaho Medical Association. Dr. Smith retired in 1971.

Wallace E. Allen, '36, Modesto, CA, is working for World Explorer Cruises as ship's doctor aboard the S.S. Universe.

V. Terrell Davis, Jr., '36, is director of psychiatry at the Wilmington Medical Center and honorary clinical professor of psychiatry at the Thomas Jefferson University School of Medicine, Wilmington, Delaware.

William H. Jacobson, '36, Palm Springs, is the medical consultant to the Indio, California, Methadone Clinic.

Carl W. Smith, '36, Orinda, CA, had a triple coronary bypass and is doing very well. Dr. Smith has plans to do some commercial fishing.

Hastel L. Townsend, '37, Anchorage, KY, is retired. He was the director of radiology at the Louisville Baptist Hospitals.

Charles Eckert, '39, was presented the Distinguished Service Award of the American College of Surgeons. Dr. Eckert was cited for "his contributions to better care of the surgical patient, especially those suffering from malignant disease . . . and for unselfish service to surgery . . . ."

'40s

George S. Loquvam, '42, Talent, OR, has retired from the Western Laboratory and the Institute of Forensic Sciences, Oakland, California, to a small farm in Oregon.

Louis A. Gottschalk, '43, Orange, CA, is professor and co-director of the National Alcoholism Research Center, Department of Psychiatry and Human Behavior at the University of California, Irvine, College of Medicine.

Jacob Kraft, '44, elected to a second term as president of Police Physicians and Surgeons.

Theodore J. Smith, '46, has left his practice in Tacoma to accept an appointment with the U.S. Air Force as Chief of Internal Medicine at Davis-Monthan AFB in Tucson.

David S. Johnson, '48, Portland, OR, spent three months on sabbatical in London at the Institute of Ophthalmology and Moorfields Eye Hospital, studying ocular pathology.

John A. McFarlane, '48, Sioux City, IA, spent last summer at a Mission Hospital in Gaza doing volunteer medical work.

Russell D. Shelden, '49, is a clinical professor of anesthesiology at the University of Missouri School of Medicine, Columbia.

'50s

Robert Obourn, '50, Topeka, KS, was appointed Mary E. Taylor Professor of Clinical Psychiatry in the Menninger School of Psychiatry.

Ralph T. Streeter, '50, Indianapolis, was elected to the executive board of the National Abortion Rights Action League.

Noboru Oishi, '53, director of the Clinical Science Program, Cancer Center of Hawaii, was promoted to professor of medicine, John A. Burns School of Medicine, University of Hawaii.

David H. Corser, '54, is chairman of the pediatric department of Skemp-Grandview-La Crosse Clinic, a multiple-specialty clinic in La Crosse, Wisconsin.

Selma Kaplan, '55, San Francisco, was listed in the book entitled Best Doctors in the U.S. Dr. Kaplan is a pediatric endocrinologist.

Jules A. Kernen, '55, was last year's president of the Los Angeles Society of Pathologists.

Stanley M. Galas, '56, has retired from active duty, and is an associate of Dr. Dennis Shepard, Santa Maria, California.

Paul L. Friedman, '57, St. Louis, is president of the Missouri Society of Anesthesiologists and was appointed director of ob/gyn at St. Mary's Health Center.

Ralph H. Harder, '57, Jackson, CA, is chief of staff at the Amados Hospital, and is on the board of directors at Colit Academy of Family Physicians.
Emil L. Mantini, '58, Clarksburg, WV, was recently invited to be a founding member in the North American Society for Pacing and Electrophysiology. The selection to membership was limited and based on the contribution to cardiac pacing and electrophysiology.

'60s

Joseph A. Sisson, '60, is chief of lab service at the V.A. Medical Center, Hampton, Virginia, and professor of pathology, Eastern Virginia Medical School.

Phillip E. King, '61, became board certified last year and is in practice in Johnstown, Pennsylvania.

John D. Rich, '62, was appointed chief of the plastic surgery service at Fitzsimons Army Medical Center, Denver.

Thomas D. Petersen, '64, San Diego, is chief of orthopedics at Alvarado Community Hospital.

Carolyn B. Robinowitz, '64, Bethesda, MD, was reelected vice president of the Council of Medical Specialty Societies. Dr. Robinowitz also is director of the American Board of Psychiatry and Neurology.

Carl G. Kardinal, '65, was the "Guest Editor" of the December 1979 issue of Seminars in Oncology, which was devoted to "Historic Milestones in Cancer Research."

Robert B. Telfer, '65, Daly City, CA, is the representative from the Department of Neurology to the University of California, San Francisco Clinical Faculty Association.

Thomas J. Prendergast, '66, Irvine, CA, has been director of the Division of Epidemiology and Disease Control, Orange County Public Health for nearly three years. Dr. Prendergast says, "classmates, alumni and others may rest assured that their health has been safeguarded at Disneyland, Knott's Berry Farm and Lion Country Safari. But in L.A. County you take your chances."

Gary S. Rachelefsky, '67, Los Angeles, CA, was appointed to the Editorial Board of Pediatrics for three years.

Joel M. Karlin, '68, Lakewood, CO, was elected president of the Clear Creek Valley Medical Society, which is the second largest county medical society in Colorado.

Charles L. Rich, '69, is assistant professor of psychiatry at the University of California, San Diego.

James S. Roberts, '69, has been named assistant vice president for accreditation by the Joint Commission on Accreditation of Hospitals (JCAH). He also is a member of the American Society of Internal Medicine, the American Public Health Association and is listed in Who's Who in Health Care.

'70s

Bruce D. Fisher, '70, Plainfield, NJ, is chief of infectious diseases at Muhlenberg Hospital in Plainfield. He also is clinical assistant professor of medicine at Rutgers Medical School.

Donald R. Graham, '70, is an Epidemic Intelligence Service Officer for the Hospital Infections Branch of the Center for Disease Control in Atlanta.

Clifton G. Harris, III, '70, has established a practice in vascular and general surgery with the Santa Cruz Medical Clinic in Santa Cruz, California.

David W. Orbals, '70, St. Louis, was elected to fellowship in the American College of Physicians. Dr. Orbals has a private practice in internal medicine and infectious diseases.

Paul C. Simpson, Jr., '70, is an assistant professor of medicine at the University of California, San Francisco.


William K. Summers, '71, is on full-time faculty in the Department of Psychiatry and the Department of Medicine at the University of Southern California.

Peter Glickman, '74, Placentia, CA, was recently certified by the American Board of Ophthalmology.

Peter L. Jacobson, '77, is the chief resident in neurology at North Carolina Memorial Hospital, Chapel Hill.

Allan Yo, '77, San Francisco, would appreciate cards and letters from his classmates to help cheer him up during a long illness.
**Former House Staff**

Stephen Banko, M.D., Mansfield, OH, was elected in 1979 to charter commission in city government, and is a member of the PPRO Finance Committee.

Paul Goodnick, M.D., Bronx, NY, received the Resident Research Award in the New York District A.P.A.

Leopold Hofstatter, M.D., St. Louis, presented a paper at the American Meeting of the Southern Medical Association in Las Vegas. He also was the invited keynote speaker at the 1st World Congress on Limbic Epilepsy.

James D. Morrissey, M.D., Stockton, CA, was on the American-Nepalese joint expedition to Guari-Shankar last spring.

John S. Spratt, Jr., M.D., Louisville, is editor of the *Louisville Medicine*, and presented a paper on the "Epidemiology of Screening for Cancer" at the annual meeting of The American Cancer Society Professors of Clinical Oncology, at Ft. Lauderdale in November.

Brian H. Weinerman, M.D., has been head of the hematology-oncology section at St. Boniface General Hospital, University of Manitoba, Winnipeg, since 1976.

**In Memoriam**

Edward R. Askew, '77 .......... October 25, 1979
James H. Barnes, '77 .......... December 28, 1979
John H. Basham, '36 .......... April 23, 1979
Adam N. Boyd, '26 .......... March 17, 1979
Joe M. Boyles, '30 .......... May 21, 1979
William L. Clothier .......... May 11, 1979
John R. Cochran, '31 .......... August 24, 1979
Jerrold P. Commons, '52 .......... July 25, 1979
Louie H. Fuson, '15 .......... August 22, 1979
William H. Geistweit, '19 .......... June 13, 1979
Marvin H. Gibstine, '46 .......... August 15, 1979
Edward R. Grose, '33 .......... July 2, 1979
Milton S. Grossman, '57 .......... August 26, 1979
Otto H. Grunow, '40 .......... December 5, 1979

Landon H. Gurnee .......... March 20, 1978
H. Clagett Harding, '43 .......... September 30, 1979
John R. Haslem, '33 .......... September 9, 1979
Dwight L. Hood, '28 .......... October 16, 1979
Lloyd F. Kaiser, '31 .......... July 19, 1979
Clyde E. Kane, '30 .......... December 15, 1979
Walter R. Langston, '35 .......... June 24, 1979
Robert S. Leggett, '33 .......... May 1, 1979
Irwin Levy .......... August 28, 1979
George R. Magee .......... March 26, 1979
John A. Moncrief .......... June 25, 1979
T. F. O'Conner .......... December 12, 1979
Albert L. Olsen, '31 .......... November 23, 1979
Oakley K. Park, '40 .......... September 12, 1979

Walter S. Priest, '20 .......... December 1, 1979
Verne R. Ross, '28 .......... September 8, 1979
Charles R. Rountree, '24 .......... November 11, 1979
John C. Schmidtke, '26 .......... September 25, 1979
Sam Schneider, '36 .......... August 23, 1979
Henry C. Shaw, '29 .......... September 20, 1979
James N. Sledge, 43D .......... October 15, 1979
James O. Threadgold, '26 .......... July 19, 1979
Edmund H. Werling, '30 .......... June 21, 1979
Ray D. Williams, '37 .......... October 21, 1979
A common loon getting down to a basic drink of water was photographed by F. Glenn Irwin, M.D., class of 1930. One of Irwin's hobbies is wildlife photography. He is now semi-retired, lives in Decatur, Ill., and is looking forward to the 50th reunion of his class in May 1980.

Students and alumni are invited to submit their photos and artwork for possible use in Outlook. Call or write for information.