1985

Outlook Magazine, Spring 1985

Follow this and additional works at: http://digitalcommons.wustl.edu/outlook

Part of the Medicine and Health Sciences Commons

Recommended Citation

This Article is brought to you for free and open access by the Washington University Publications at Digital Commons@Becker. It has been accepted for inclusion in Outlook Magazine by an authorized administrator of Digital Commons@Becker. For more information, please contact engeszer@wustl.edu.
Molecular Modeling — No-Test-Tube Chemistry
The era of rigid, ball-and-stick modeling of chemical compounds' three-dimensional structure has been laid to rest by the advent of the small computer. Several computers can be electronically linked to solve complex computing problems generated by the variety of shapes that molecules can assume.
On the Cover:
Electronic models of molecules enable chemists to more accurately predict potentially important biological interactions. Here, the computer video screen shows a color display of a compound under study. To investigate interactions between that molecule and other structures, the electronic image can be manipulated with the computer's joystick, thus bypassing traditional bench research.

Spring 1985
Volume XXII, Number 1
Outlook Magazine (ISSN0195-0487) is published quarterly by the Washington University School of Medicine at 660 S. Euclid, St. Louis, MO 63110. Second-class postage paid at St. Louis, MO.
Direct alumni news and all other communications to the editor, Outlook Magazine, 660 S. Euclid, St. Louis, MO 63110.

© Washington University
School of Medicine

Permission is granted to reproduce materials contained herein, provided Outlook, the Magazine of Washington University School of Medicine is credited.
Drugs by Design

BY SUZANNE HAGAN

A plant extract, used by aborigines to coat their arrows with a curare-like substance, has helped to pave the way for rational design of pharmaceutically valuable drugs. In the process, the traditional methods of drug discovery — trial and error, or serendipity — have given way to the era of computer-designed drugs.

Picrotoxin, the ancient arrow poison that launched a research effort at the School of Medicine to develop a better drug for the treatment of epilepsy, is a product of plants in the Menispermaceae family. These plants, whose romantically sounding name — "moonseed" — belies their deadly properties, are more commonly found in the tropics than in temperate climates.

Picrotoxin's "sibling" is a naturally occurring substance, a neurotransmitter that suppresses stimulation of brain cells. The chemical kinship between picrotoxin and its natural counterpart causes brain cells to embrace the moonseed mimic, with deadly results.

Convulsion-causing picrotoxin might seem to be an unusual starting place from which to launch a search for an anti-epileptic drug. But as the molecule's three-dimensional structure was pieced together — and that of the site to which it binds on the nerve cell's surface — this paradox began to make sense.

Epilepsy, a disease affecting more than four million Americans, is a disturbance in the brain's normal electrical activity. Scientists believe that if they can learn more about the architecture of the brain cells' surfaces — and especially, that specific area of the cell surface to which neurotransmitters attach — then they can design better drugs for neurological diseases, including epilepsy. Picrotoxin's similarity to a natural brain substance causes brain cells to recognize the poisonous imposter. But if a chemical could be designed that is similar enough to picrotoxin that brain cells accept it, but dissimilar enough so that it blocks — rather than causes — a convulsion, then this might be a valuable new tool in the armamentarium of anti-epilepsy drugs.

Ironically, there are many types of drugs effective against the various forms of epilepsy, but how these drugs work is still a mystery, for the most part. And it's impossible to scientifically design drugs to do a specific job unless the architecture of the part of the cell membrane to which the drug attaches — its receptor — is known. In a scientific version of the "chicken-or-the-egg" conundrum, cellular architecture is inferred by looking at the...
drug that "fits" a certain area on a cell's surface — "Like designing a hand by looking at the shape of a glove," says Garland Marshall, Ph.D., professor of biological chemistry. "We are really trying to be three-dimensional code breakers. Each drug represents an example of a message we're trying to decode. Then you can use that code as a pattern and compare the differences in drug structure with their potency."

Marshall, who is also professor of physiology and biophysics, designs the computer programs (software) that are used to deduce the structure of "biological hands" — the receptors on a cell membrane. Once the hand's structure has been deduced (by analyzing the three-dimensional shape of its "glove" — the drug that binds to it), it can be used to design the structure of new, better-fitting gloves — chemicals likely to bind even more closely than the natural glove.

"What we're doing is molecular recognition — how one molecule looks to another," says Marshall — a sort of not-test-tube chemistry. By developing molecular models that can be manipulated on the video screen of a computer terminal, Marshall can quickly predict the likelihood of a good "fit" between new drugs and their receptors.

The era of rigid, ball-and-stick modeling of chemical compounds' three-dimensional structure has been laid to rest by the advent of the small computer, and especially, by the ability to link several computers to solve complex computing problems generated by the infinite num-
ber of shapes that flexible molecules (or large molecules) can assume.

"One of the things I've learned," muses Marshall, "is that physical chemistry is not nearly as complete as I naively believed as a student. The complexity of biological systems is such that there are many things that are dimly understood. It's only by trying to model something on a molecular level that you have to come to grips with these phenomena. You have

---

Scientists believe that if they can learn more about the architecture of brain cells' surfaces — and especially that specific area of the cell surface to which neurotransmitters attach — then they can design better drugs for treating neurological diseases.

to stop waving your hands over them and saying, 'Of course, it's a hydrophobic interaction.'"

And in the course of constructing molecular models, Marshall can save traditional chemists months or years of wasted time by being able to accurately predict what will work — and what won't. This is how he made a believer out of his colleague Douglas Covey, Ph.D., associate professor of pharmacology, some years ago.

Now an enthusiastic convert to electronic chemistry, Covey agreed to help William Klunk, a former student with a background in chemistry, develop a new pharmaceutical drug for the treatment of epilepsy. Although currently available drugs provide substantial benefit in the treatment of epilepsy, some are effective against only certain types of seizures. Others with a broader spectrum of anticonvulsive activity have undesirable side effects. Thus, more specific drugs are needed for improved medical treatment of epilepsy.

Klunk knew that one set of drugs, whose structure resembles picrotoxin, looked promising as a starting point: By adding chemical sidechains to the drugs' "skeleton," he might be able to come up with a derivative that would block convulsions more effectively than any of the currently used drugs.

With a system developed by Marshall, and the pharmacological expertise of Covey, Klunk (who last May, earned an M.D./Ph.D.) succeeded in making a new drug that was very effective in blocking convulsions in animals.

James Ferrendelli, M.D., professor of pharmacology and neurology, was Klunk's thesis advisor. Ferrendelli summarizes the technique's effectiveness:

"You can look at a drawing of a molecule on paper, but that tells you nothing about how it behaves. And with so many potential compounds to test, it's too difficult and time-consuming to process by human inspection." Thus, the computer adds the speed and precision missing from traditional drug discovery, testing, and development of analogues — the "me-toos" — that are such an economic incentive in drug companies' efforts to market newer, better drugs.

Until picrotoxin was studied by molecular modeling, the structure of its biological receptor — which is near the receptor for GABA, an important inhibitory brain neurotransmitter — was unknown. Pharmacologist Covey teamed with biophysicist Marshall and student Klunk to discover that this important receptor was next to a chloride channel in the cell membrane. If a drug binds to this receptor and simultaneously blocks the chloride channel, it produces a convolution. However, if the drug's structure allows it to bind to the receptor without blocking the chloride channel, the drug prevents convulsions.

Without computer modeling, it is unlikely that this quirk in molecular architecture would ever have been recognized.

But developing an economically viable, new drug for epilepsy treatment wasn't the sole raison d'être of these efforts. And it wasn't meant to be. "We were somewhat naive," remembers Klunk's adviser Ferrendelli, Seay Professor of Clinical Neuropharmacology. "We published the news without patenting this drug. However, there is no reason to think that it might have been a better drug than
James Ferrendelli, M.D., supervised research that led to the design and testing of a new drug that successfully stopped convulsions. The drug’s design and effectiveness were predicted by computer. Computers add speed and precision to the traditional method of drug discovery — trial-and-error.

Developing new drugs is really the prerogative of industry, say Ferrendelli, Covey and Marshall. But they point out that developing the molecular models that will stimulate new drug design is really the province of the pure scientist. And it’s in the academic area where this is most likely to happen.

“It’s really unlikely that one person would have the biochemical and mathematical background to be able to design new drugs,” reflects Richard Dammkoehler, Ph.D. Dammkoehler, professor of computer science, co-developed the computer modeling system Marshall uses to create the programs that enable Covey and other pharmacologists to develop new drugs. Dammkoehler was able to show Marshall better mathematical methods for calculating how flexible molecules like peptides (small proteins) could interact with their receptors. In turn, Dammkoehler had to learn some-thing about the application of his methods — how substances interact in biological systems. This cross-campus, cross-disciplinary fertilization of ideas and knowledge has been a part of the birth of the electronic era of drug design. Inter-actions between chemicals and their biological receptors that have been predicted to work, based on computer models, have worked; those that have been predicted to not work, haven’t.

In the future, other traditionally known drugs like picrotoxin will enter the age of electronics. Using computer graphics to project the three-dimensional structure of a pharmacologically active substance will enable researchers to deduce the structure of the drug’s receptor. This new knowledge can then be used to selectively construct drugs that are more effective and safer to use.

For example, Covey has succeeded in designing a “suicide inhibitor”— a self-destructing precursor — for estrogen. Thus, estrogen-dependent tumors will be starved selectively, while normal cells are unharmed. Animal tests of this substance, recently studied by computer design, are being conducted by David Puett and Steven Zimniski, endocrinologists at the University of Miami (Florida). If this new drug can stop the growth of estrogen-dependent tumor cells in mice, then the next step would be to test the substance on human estrogen-dependent tumor cells. Eventually, if all goes well, clinical trials might be in the offing, to determine whether breast cancer cells that escape the surgeon’s knife can be selectively destroyed, leaving non-cancerous cells unaffected.

Joseph J. Villafranca’s group at Penn State has created suicide inhibitors for a key enzyme converting dopamine to norepinephrine. Animal tests will show whether these substances may be useful in the medical treatment of hypertension.

Thus, the goal of more selective medical therapies doesn’t seem quite so distant. The moonseed’s deadly offspring leaves a legacy of hope — hope that computer-engineered, precision pharmaceuti-cals will lead to a pharmacopeia of safer, more effective drugs.
It's 8:30 a.m. on a cold and sunny Tuesday last November. James L. Cox, M.D., chief of cardiovascular surgery at Barnes and Children's hospitals, stands over the exposed heart of a young man on an operating table. Over the heart, he holds a rectangular plaque of sixteen electrodes.

Fifteen feet of cable snakes from the electrodes, around the anesthesia apparatus, to a console in the corner of the room. Seated at the console, with only eyes visible between surgical mask and cap, electrophysiologist Michael E. Cain, M.D., waits to record electrical impulses from the young man's heart.

On the first floor of the Clinical Sciences Research Building, a quarter-mile away, Peter B. Corr, Ph.D., associate professor of medicine and pharmacology, sits with his feet up. Gazing at his computer connected to the operating room by 2,000 feet of fiber optic cable, he seems frustrated at the delay.

The young man on the table is oblivious to the green-robed figures around him, the bypass machine at his feet, and the two giant screens displaying his heart rhythm on either side of the room. For him, this is the end of a long journey, which began with a childhood attack of rheumatic fever.

The infection scarred a heart valve, impeding the flow of blood from the atria (upper chambers) to the ventricles (lower chambers) and causing his atria to gradually enlarge. Then a loop of tissue in the right atrial wall began to short-circuit, causing his heart to race at 300 beats per minute.

Hopefully, this surgery will enable the young man to live his life at home in the mountains of Kentucky, free from an abnormal heart rhythm. But more will be required than a surgeon's knife. Cox, Cain, and Corr will use a computer to map and correct the young man's abnormal heart rhythm.

Arrhythmias, accountable for the sudden deaths of 600,000 Americans each year, kill more people in this country than all other diseases combined. And though they kill quickly, they kill prematurely. "Most victims are middle-aged men and, to some extent, women, who are at the productive prime of their lives," says Cain, assistant professor of medicine.

"But for the abnormal rhythms, their hearts would continue to function for another 10, 20, or 30 years."

An abnormal rhythm is any deviation from the rate or regularity of a normal heart beat. An example is tachycardia (rapid beating of the heart), which had brought the young man from Kentucky to the operating room at Barnes Hospital.

Tachycardias occur when an electrical impulse arising at the heart's pacemaker node is diverted from its normal pathway through the heart, or when impulses arise from sites outside the pacemaker (see p. 11). Tachycardias involve the whole heart but originate in either the atria or ventricles. Most atrial tachycardias are fairly harmless, but ventricular tachycardias are often associated with sudden death.

Many abnormal rhythms can be controlled with medication — if a patient survives an initial episode or is resuscitated after the heart stops beating. But some patients fail to respond to medication, and so they become candidates for surgery. Surgery also spares young patients from a lifetime of medication.

One of Cox's most memorable surgical candidates was a 28-year-old Swedish airline pilot, a strapping man in good health except for a cardiac abnormality called Wolff-Parkinson-White syndrome (see p. 11). One day, the pilot was fishing on a pier when his heart developed an abnor-
normal rhythm and stopped beating. Although the rescue squad did not reach him for fifteen minutes, he was resuscitated, regaining consciousness six weeks later. Cox flew to Sweden and surgically corrected the abnormal rhythm. Now the man need not worry that he will die suddenly while fishing—or piloting.

Before a surgeon can correct an abnormal rhythm, an electrophysiologist must determine the site of abnormal activity by mapping the heart. At Washington University, preliminary mapping is carried out prior to surgery in the Clinical Electrophysiology Laboratory at the School of Medicine. A catheter inserted into the heart via a leg vein contains electrodes that provoke abnormal rhythms and record the heart's activity. However, catheterization reveals only the approximate area of abnormality because it involves only four stationary electrodes.

Detailed mapping of the abnormal area is possible once the heart is exposed. At other institutions, the map is made by moving a single electrode from one part of the heart to another. This method has two disadvantages. It is very time consuming, requiring the patient to be maintained on a heart-lung bypass machine during mapping and subsequent surgery. Moreover, the electrophysiologist sometimes finds it impossible to maintain the heart in an abnormal rhythm long enough to complete the map.

"A second problem," says Cain, "is the assumption that the rhythm is always the same when you put the probe on one site and two minutes later put the probe on another. But in over 25 percent of cases, the rhythm is so irregular that every beat is different."

About five years ago, Corr and Cain realized that a computer could solve both problems, enabling data to be recorded and stored from many different electrodes simultaneously. A map of any area of the heart—a record of actual events during a single heartbeat—could be made in just a few minutes.

Needed then was a computer that could store vast amounts of information. If 240 electrodes are used to map the heart, 6 million bits (digital data points) are generated every second. "So even with a very large disk," says Corr, "you only have a storage capacity of seconds. We need a storage capacity of at least an hour. Interestingly, the solution came from the space program. We called the people at NASA in Houston and ended up buying a special type of tape recorder."

For the next two and a half years, Corr and former engineer Francis X. Witkowski, M.D., Ph.D., assembled the recorder and other components into the present system. The cost of the computer, the console in the operating room, and an experimental animal facility was $300,000. Private companies donated most of the money.

The researchers also had to design electrodes to fit the heart. In addition to rectangular plaques, they made bands that encircle the heart; fine needles that pierce the heart and record across the wall; and "socks." Made of cloth, a sock (which stretches over the heart) is dotted with 48 teflon button electrodes.

On July 1, 1983, just after Corr and Witkowski had completed the computer system, Cox came to Washington University, hopeful that his collaboration with the other researchers would lead to a reduction in the number of sudden deaths from abnormal heart rhythms. The team conducted their first operation at Barnes Hospital in August 1983. But no one had tagged a number to the operation on Tuesday, November 20, 1984.

\textbf{ANSWERS GENERATE QUESTIONS}

At 9:00 a.m., Corr sits in front of the computer, which is about the size of a freezer. Above his head 9,000 ft. of one-inch tape is ready to unwind at the rate of 30 inches per second. To his right, surgical resident and research fellow in cardiol-
Michael E. Cain, M.D., is the electrophysiologist who records electrical impulses during surgery for correction of abnormal heart rhythm. He is responsible for inducing tachycardia so that the source of aberrant electrical activity can be pinpointed, and he must also restore normal rhythm to the heart between episodes of tachycardia.

Jeffrey Kramer, M.D., sits at the computer's keyboard, ready to analyze data from the operating room.

At 9:05, Corr and Kramer spring into action. Corr, in touch with the operating room via headphones, hears that Cox has positioned three plaques of electrodes on the young man's atria. "Let's go," he shouts to Kramer, who starts typing furiously on the keyboard. Suddenly, a green trace of the heart beat flows across the monitor, and the tape recorder whirrs, recording this electrocardiogram.

Thirteen minutes later, Cain has induced tachycardia through a stimulator sutured to the young man's heart. For a few seconds, the heart pulses wildly under the steel and blue overhead lights. Then Cain urges it back into its normal rhythm, and Cox moves the plaques of electrodes to a second set of positions. (Normally, the three plaques cover the atria at one time, but this patient's atria were greatly enlarged.)

By 9:40 the electrodes are in place, the computer is prepared for a new onslaught of information, and Cain again paces the heart with extra beats. In the computer room, the electrocardiogram on the display monitor quickens as the heart goes into its rapid routine.

By 9:43, the screen displays traces (electrograms) from 44 electrodes. Moving closer, Corr holds up his pencil to assess which electrode first detected electrical activity. That will probably be the
Peter B. Corr, Ph.D., helped assemble the recorder needed to store the vast amounts of data generated during surgery. In touch with the operating room via headphones, he tells the surgeon the precise site from which abnormal beats originate.

site of the atrial loop. "What do you think, Mike?" he says to Cain over the intercom. "Nine to 16 are all late, 18 looks early, and 25 to 32 are late. Oh, look at 37, Mike — that has to be the earliest."

Ten minutes later, the printer spews out several feet of data confirming Corr’s assessment: The electrodes connected to channel 37 detected an impulse .064 second after the beginning of the recording. The other electrodes detected activity later.

During the next hour, Cox drains blood from the heart and opens the right atrium. Cain, Corr and Kramer then map the wall between the two atria to make sure that the impulse at site 37 had not originated inside the heart, out of reach of electrodes on the surface. And while Cox performs the surgery, Corr analyzes the electrograms from the normal heart beat re-
corded earlier, confirming that the abnormal site is separate from the heart’s pacemaker node. “This is an example of how valuable our system is,” he says.

“We decided to go back and look at the normal rhythm [that the patient had] before he went into tachycardia. We had only one chance to do that. It happened 45 minutes ago. With all this recording capability, we could retrieve it.”

Assured that he was not about to damage the pacemaker node, Cox freezes the small piece of abnormal heart muscle with a pencil-shaped cryoprobe. That site would never again short-circuit impulses. Later, Cox also repairs the young man’s damaged heart valve.

A few days after the operation, Cox (who is head of cardiothoracic surgery) muses on future plans. “Our next step is to map the entire heart, inside and out, in a single beat, without opening the ventricles. Since the walls of the ventricles are so thick, the map would require a three-dimensional array of 160 electrodes — 40 needles with 4 electrodes on each needle. Hopefully, we will develop this system by next summer by adding more channels to the console in the operating room.

“We would also like to develop a screening program, using the computer and just the standard electrocardiogram, that would detect those persons at risk of imminent sudden death.”

Cain is already at work on such a project. To date, he has subjected the electrocardiograms of persons with histories of ventricular tachycardia to Fourier analysis. This corrects for normal waves, highlighting abnormalities. Cain has already detected one abnormality that cannot be seen by eye. Further studies will allow him to pinpoint its significance. If it predicts ventricular tachycardia, mass screening would enable persons at risk to be medically or surgically treated.

Says Cox: “I think that with the computerized mapping system that Corr developed, Cain’s expertise, and our experience operating on patients with ventricular tachycardia, that we have a good chance to make a dent in those 600,000 deaths.”

Heart Rhythm: Where the Beat Comes From

Heart beats (contractions of the muscular heart) are induced by electrical impulses generated within the heart. Normally, an impulse arises at a specialized group of cells (the pacemaker node) in the right atrium. It then passes through a bundle of conducting cells to the larger and more powerful ventricles. Thus the atria contract first, squeezing blood into the ventricles. Then the ventricles contract, pumping blood into the arteries.

Abnormal heart rhythms, both atrial and ventricular, have two modes of origin. A site in the wall may generate irregular or rapid impulses additional to the impulses produced by the pacemaker node. Or, an impulse arising at the normal site may follow an abnormal pathway.

The second mechanism operates in persons with Wolff-Parkinson-White (WPW) syndrome, which affects about 1 in every 1,000 people. WPW patients have a Kent bundle (an extra tract of conducting tissue) between their atria and ventricles. Most of the time the Kent bundle merely doubles the normal pathway, causing no problem. But occasionally, it allows an impulse that has reached the ventricles to travel back up to the atria. The impulse continues to loop between chambers, like a dog chasing its tail. The heart beats every time the circuit is completed.

With the aid of the computer, Cain and Corr can determine exactly where the Kent bundle enters the atria and ventricles. Then Cox can make an incision between the two points, severing the Kent bundle and preventing it from conducting electrical impulses.

Loops of electrical activity may be responsible for some ventricular tachycardias. Many people have damaged portions of heart tissue due to a blockage of the coronary artery, and such an infarct may delay an impulse. By the time the impulse finally escapes the damaged area, the surrounding normal heart muscle is capable of being stimulated again, and the impulse loops between the two areas. One cure is to locate the troublesome site and surgically destroy it. Ventricular tachycardias need to be prevented because they can degenerate rapidly into irregular, quivering movements called ventricular fibrillation. A fibrillating heart is unable to pump blood, causing loss of consciousness and possibly, death.
WHEN FEAR STRIKES

By Suzanne Hagan

When Tom Tlapek sat down to take his final exam in history that spring day in 1974, little did he realize that it would mark a turning point in his life. Not because of his exam grade, but because of something that happened just as he was finishing.

"I was writing away," he remembers, "when all of a sudden, for no apparent reason, my heart started to race. I could hardly breathe. I got to feeling very fearful, and I got scared - really scared. I thought I was having a heart attack, so when I came out, a friend took me to the hospital near campus. They gave me a physical and told me there was nothing wrong - I wasn't having a heart attack. I left for home still wondering what had happened."

This episode was only the first of a series, as Tlapek was soon to find out. These sudden, unexplained occurrences began to happen daily. "I was really bewildered and wondered 'what is going on?'" he remembers. "I was exhausted, so that summer, my parents and I decided the best thing was for me to just take some time off - to not work, just laze around the pool and play golf, in hopes that this would help."

But what was wrong with Tlapek would take more than R&R to fix. He kept having the attacks, which caused him to withdraw - from friends and his normal activities - out of fear he'd have another episode. The fatigue that set in, and the resultant depression, completed the vicious circle. "I was too embarrassed to talk to anyone about it," he admits. But deep down, he felt that his problem wasn't just psychological - it had a physical basis, he was convinced.

So Tlapek set out on a quixotic search for the cause of these periodic attacks that left him so debilitated. His quest was to prove long - and costly. Bouncing from one medical practitioner to another - a heart specialist, then an ear specialist, and a general practitioner - and going to Gestalt therapy proved only moderately helpful. His illness remained undiagnosed.

Then, about two years ago, he saw a television program that gave a name to his problem: panic disorder, or anxiety neurosis.

Armed with this information, Tlapek was nearly finished tilting at windmills. After calling Washington University's library, he was referred to the medical center hospitals, where psychiatrists listened to his tale, diagnosed his illness and prescribed an antidepressant medication which he takes daily. That medication, plus a greater self-awareness Tlapek gained during his therapy, has ended his quest for relief from the curse of unpredictable panic attacks. But the search for the underlying cause is, in some ways, off to a fresh start.

SOLDIER'S HEART

Known since before the Civil War era, panic disorder has been given a variety of names over the centuries, including "soldier's heart," a reference to the exhaustion that overtakes its victims when they embark on any prolonged physical exertion. The poet Shelley is thought to have had an anxiety attack that prompted these lines in *Indian Serenade*: "O lift me from the grass! I die! I faint! I fail! My cheek is cold and white, alas! My heart beats loud and fast." The cause of this syndrome was the subject of much speculation. Badly adjusted soldiers' packs and hard field service, wounds and injuries were suggested by physicians in the 1860s. Heart problems, notably a heart that was too small, were also cited by 19th century practitioners. Freud thought that coitus interruptus and masturbation were the cause, and one imaginative doctor believed that anxiety attacks represented the..."
Tom Tlapek permitted researchers to induce a panic attack, ultimately demonstrating a biological basis for these attacks.

Epidemiologists at the National Institute of Mental Health (NIMH) estimate that 13.1 million Americans suffer from anxiety disorders, with about 1.2 million afflicted with panic disorder. But psychiatric disorders are much harder to definitively diagnose than medical illnesses. And many persons develop complications, or have coexisting illnesses, that confound research results. How could persons with panic disorder be distinguished from those with other anxiety syndromes?

For several years, it has been known that a chemical — sodium lactate — can precipitate the symptoms of panic attack when infused into the bloodstream. This chemical brings on an attack in most, but not all, persons who are susceptible to this disorder. But panic disorder may be a complication of other psychiatric illnesses, such as schizophrenia. Researchers need to study a group of patients with only anxiety neurosis. Thus, Eli Robins, M.D., Wallace Renard Professor of Psychiatry at Washington University School of Medicine, and Kevin Butler, M.D., chief resident in psychiatry, selected a group of patients without complicating factors; this group included Tlapek.

Robins and other researchers became convinced that Tlapek's intuition was correct, that there was a difference in the brains of patients who had panic attacks that would be apparent if the right kind of radiological study was performed.

Together with other patients subject to panic attacks, Tlapek allowed Butler to infuse a lactate solution into one of his veins and observe the results. A radioactive marker was also infused, so that an image of the brain could be taken with a PET scanner. Pictures of Tlapek's brain, and those of other patients, revealed a startling difference when compared with

fantasy of giving birth. Haldane and Priestley, writing in 1935, attributed "neurocirculatory asthenia" (another term for panic disorder) to "fatigue of the nervous system" due to "nervous overstrain" and "infections" and associated with "imperfect oxygenation of the blood."

Epidemiologists at the National Institute of Mental Health (NIMH) estimate that 13.1 million Americans suffer from anxiety disorders, with about 1.2 million afflicted with panic disorder. But psychiatric disorders are much harder to definitively diagnose than medical illnesses. And many persons develop complications, or have coexisting illnesses, that confound research results. How could persons with panic disorder be distinguished from those with other anxiety syndromes?

For several years, it has been known that a chemical — sodium lactate — can precipitate the symptoms of panic attack when infused into the bloodstream. This chemical brings on an attack in most, but not all, persons who are susceptible to this disorder. But panic disorder may be a complication of other psychiatric illnesses, such as schizophrenia. Researchers need to study a group of patients with only anxiety neurosis. Thus, Eli Robins, M.D., Wallace Renard Professor of Psychiatry at Washington University School of Medicine, and Kevin Butler, M.D., chief resident in psychiatry, selected a group of patients without complicating factors; this group included Tlapek.

Robins and other researchers became convinced that Tlapek's intuition was correct, that there was a difference in the brains of patients who had panic attacks that would be apparent if the right kind of radiological study was performed.

Together with other patients subject to panic attacks, Tlapek allowed Butler to infuse a lactate solution into one of his veins and observe the results. A radioactive marker was also infused, so that an image of the brain could be taken with a PET scanner. Pictures of Tlapek's brain, and those of other patients, revealed a startling difference when compared with
Eli Robins, M.D. (left), and Kevin Butler, M.D., interview a patient. Robins and Butler selected a group of patients with panic disorder uncomplicated by the presence of other psychiatric conditions. This “pure sample” group permitted researchers to undertake a meaningful radiological study to pinpoint the cause.

Images of the brains of normal persons.

“Data from the PET scan showed a marked difference in blood flow between the right and left sides of a specific part of the brains of patients in whom lactate provoked a panic attack,” explains Marcus Raichle, M.D., professor of radiation sciences at the Mallinckrodt Institute of Radiology. “This asymmetry is located in a region of the brain that is believed to control emotions,” concludes Raichle, who is also professor of neurology.

The asymmetry is consistently seen in patients who are vulnerable to lactate-induced panic attacks. It is never seen in normal volunteers.

And this research is thought to be important for more than just panic disorder. Other psychiatric illnesses, such as schizophrenia and depression, are also believed to have a biochemical or biological basis. Jeffrey H. Boyd, M.D., an expert in the epidemiology of panic disorder who works at NIMH, calls the Washington University team’s research “… exciting — there is a tremendous need to localize abnormalities in the brains of those with panic disorder. This research is striking and should inspire researchers to look in [that] region for specific abnormalities in the area.”

Measurements of blood flow were taken on both sides of the brain in seven areas suspected of mediating anxiety. Only one of these areas — the parahippocampal gyrus — displayed an imbalanced blood flow in all patients who had a history of panic disorder and developed symptoms when they were infused with lactate.

**MIMICS HEART DISEASE**

But to those who have anxiety neurosis, getting the word out about “their disease” is of paramount importance. Tom feels a great sense of relief, and vindication, to learn that his suffering stemmed from a biological difference in his brain, that his symptoms were not just psychological. “If there’s one thing I’d like people to know,” he says, “it’s that this disease can be overcome.”

“Panic disorder is common,” says Eric Reiman, M.D., instructor in psychiatry at the School of Medicine. “It affects two to five percent of the population, with females being affected twice as commonly as males. The syndrome is characterized by recurrent anxiety attacks which occur suddenly and at unexpected times,” continues Reiman, an investigator on the panic attack study. “Sudden episodes of severe apprehension or fear are accompanied by a variety of unpleasant sensations. These include shortness of breath, choking, chest pain, heart racing, dizziness, trembling, sweating and tingling in the hands or feet. Since these persons often think they’re having a heart attack, cardiologists frequently see them. Persons with panic disorder may comprise 10 to 12 percent of a heart specialist’s practice.”

Tlapek’s reaction to his attacks fits this profile perfectly. And he also developed one of the common complications of panic disorder — agoraphobia (fear of leaving the house). In fact, many persons with undiagnosed panic disorder are treated in phobia clinics, with limited success. Unless their underlying, frequently unexpected anxiety attacks are recognized, the basis for the phobias that develop will be undiscovered — and remain untreated. Tlapek knows from bitter experience that the longer it takes for diagnosis and treatment, the worse the situation.

“It’s like pouring gasoline on a fire,” he says. “Your heart begins racing, and the fear you feel — the fear that you’re going to die — only causes your heart to beat more wildly.”

But panic disorder, unlike other psychiatric diseases, rarely leads to death. Instead, those who suffer from it react much the way Tlapek did: they withdraw from their friends and normal activities, often developing agoraphobia and becoming depressed. Now 32, Tlapek had his first panic attack a decade ago, when he was a college junior. His age was typical,
Since the syndrome's onset appears during late teens or early twenties.

Tlapék's medication and greater self-knowledge have kept him free of spontaneous panic attacks for the past two years, but he knows that he is not cured. Although he takes imipramine daily, he readily developed anxiety symptoms when Robin's team infused lactate into his blood. ("It was the worst one I've ever had.")

Up to 25 percent of close relatives of persons with panic disorder will display symptoms. And the knowledge that this disease is more common among family members of those afflicted with panic disorder than the general population caused Tlapék and his wife to have some second thoughts about starting a family. But only briefly.

"This isn't like giving your child a genetic disease such as hemophilia or cystic fibrosis," he asserts. "This is something that can be controlled — once it's diagnosed." Tlapék works steadily now, two days a week as a sales engineer designing heating equipment, and three days a week designing electronic controls and other equipment for military contractors. It's a busy time for him, trying to start his own business. But he pays more attention to the little signs that his body gives him when extreme fatigue or stress — past precipitators of panic attacks — signal that he's pushed himself beyond his own psychological "safe point." "I try to get lots of sleep," he says, "and I exercise — either running a couple of miles or going to aerobics classes — several times a week."

Even though his own illness is under control, Tlapék's empathy for his fellow sufferers is strong. He points out the need for a support group for persons who suffer from this disease: "I've got one friend," he remarks, "who hasn't left St. Louis for 10 years. I've offered to go with him, and he agreed, but we've never done it." Even today, Tlapék sometimes has to force himself to go to church or to a football game — anywhere where there's a crowd which, in the past, was the setting for one of his attacks.

**The Right Treatment**

Tlapék and other persons with panic disorder have an illness which can be distinguished from other anxiety conditions: panic disorder is effectively treated with such medications as imipramine, phenelzine and alprazolam, but not the typical sedatives such as valium.

"Patients' responsiveness to these drugs, plus the fact that an attack can be triggered by IV infusions of lactate, distinguishes panic disorder from other anxiety syndromes," remarks Butler. "No one knows what it is about lactate that precipitates an attack. But it does give us the opportunity to study this in a laboratory without having to wait for a spontaneous attack."

"The difference in blood flow between hemispheres," explains Raichle, "probably correlates with differences in metabolic rates. Although you might suppose that this difference is a long way from an emotional response, the activity of nerve cells is closely tied to brain blood flow because the brain stores no oxygen. Any changes in blood flow reflect differences in the activity of nerve cells on the two sides."

Raichle describes two promising areas for further research. One is the blood-brain barrier, a network of membrane-enclosed capillaries in the brain that prevents many substances in blood from reaching brain cells. "It's possible that the blood-brain barrier in persons with panic disorder is defective. In another study, we will be measuring oxygen utilization, which is the link between blood flow and the activity of nerve cells. We'll be looking at patients with panic disorder and also another group with depression. And to what extent is the movement of substances between the blood and brain restricted? Curiously enough, it may in fact be related to both of these diseases."

The results of the PET studies on persons with panic disorder were published in Letters to NATURE, Vol. 310, 28 August 1984.
ike most accidents, it happened in a split second. On December 15, 1983, Joe Swan was standing on the back of a truck, gripping a band around a lawnmower. The truck was parked at the hardware store where Swan works, and the lawnmowers were ready to be unloaded. Suddenly, the band broke and Swan flew out the back of the truck. When he landed with his arm underneath him and his hand folded under, his wrist absorbed the impact of his 260-pound body.

"It hurt," says Swan, "but at the time I didn't think there was really anything wrong with it."

Today a three-dimensional image of Swan's injured wrist is on display at the Mallinckrodt Institute of Radiology at the School of Medicine, and the image is so clear that even a lay person could guess at Swan's problem. The image shows a cluster of wrist bones, the carpals. One, a crescent-shaped carpal called the lunate, is clearly out of position.

Michael Vannier, M.D., assistant professor of radiology, created the three-dimensional picture from two-dimensional computed axial tomography (CAT) scans, using a computer technique X-rays do not give detailed information about the structure or articulation of carpals. The wrist's three-dimensional movements cannot be portrayed by single-phase X-rays.

This three-dimensional image of the wrist, achieved as an extension of earlier research on facial reconstruction in children, inaugurates a new era in the prevention and treatment of wrist injury. For the first time, researchers can get a clear picture of how movement affects the relationship of individual bones, or groups of bones, in the wrist.

X-rays do not give detailed information about the structure or articulation of carpals. The wrist's three-dimensional movements cannot be portrayed by single-phase X-rays.
wrist bones, we can do a variety of engineering tests," says Paul M. Weeks, M.D., chief of plastic and reconstructive surgery. "We can analyze the motion of those bones relative to one another and assess how much stress and strain they are subjected to. Once that is accomplished, a number of applications are obvious. One is the design of a prosthetic wrist. Another is to screen people before they go onto certain jobs to tell whether they are going to be susceptible to wrist injury. The other thing is to evaluate methods of management of wrist abnormalities."

**Stresses & Strains**

Engineering tests are already underway, thanks to the expertise of Samuel E. Logan, M.D., Ph.D., assistant professor of plastic and reconstructive surgery and mechanical engineering, and graduate student Stephen Bresina, M.S. Logan, an ex-astronaut trainee who came to Washington University last June, earned a Ph.D. in engineering from the California Institute of Technology before he became a surgeon. Bresina is a transplant from the Department of Civil Engineering at W.U. His research is supervised by Phillip L. Gould, Jolley Professor and chairman of civil engineering.

A typical day in the laboratory finds Bresina perched on a high stool in front of a wrist specimen. Three wires emerge from each of the wrist’s carpals, serving as fixed metal points that can be tracked in a magnetic field. A six-dimensional electromagnetic sensing system called a “three-space digitizer” tracks the points. A sensing antenna inside a small probe, and a transmitting antenna that lies beneath the wrist, create a three-dimensional electromagnetic field. Setting the wrist in one position, Bresina touches each fixed
point with the probe and then presses a foot pedal. Then he rotates the wrist and repeats the process. In this way he obtains sequential sets of measurements on a display monitor, and from these he can calculate each carpal's linear and angular movements during a given wrist motion.

This system was developed for use as a helmet-mounted tracker for fighter pilots when they need to fly their aircraft, track other planes, and fire missiles without looking down. It allows the positions of carpals to be measured with a precision that previously has been impossible. The data eventually go into a large Unigraphics computer (donated by McDonnell Douglas) which displays the movements of the carpals as arcs or straight lines. Moreover, the Unigraphics' CAD (computer-assisted-design) system eliminates errors introduced by movements of the radius, one of the long bones in the forearm.

The engineering studies should lead to three-dimensional models of the moving wrist. 'But,' cautions Logan, a staff member at Barnes Hospital, 'the wrist is a very complex structure with eight carpal bones of irregular shape, multiple ligaments and a number of tendons. . . so it presents a difficult engineering problem.'

Wrist Prostheses

A working model could pave the way for artificial wrist superior to current models. But a more immediate goal is the production of artificial carpals to replace individual bones. Such prostheses are already available, but they are not tailored to individual patients. 'We will be able to make a bone that would fit exactly into the slot where it belongs, rather than have a prosthesis that only comes in standard sizes, which may or may not fit perfectly,' says Logan.

The manufacture of prosthetic carpals will be possible with CAD/CAM (computer-assisted-design/computer-assisted-manufacture) technology. 'We already have the CAD portion,' says Logan. 'It's one step away from getting that image to be manufactured by a computerized tool that basically reads the computer image and gives you a three-dimensional object precisely manufactured from the three-dimensional object on the screen.'

Thus, the researchers could convert CAT scans of a damaged carpal into a three-dimensional image/blueprint for a CAM system. The latter would create a mold for an exact replica of the original bone, and the replica could then be made and used as a prosthesis. McDonnell
The two CT "slices" above are representative of the individual images used to construct the space-filling, three-dimensional picture shown on the right. Portions of the three-dimensional image can be erased so that areas in question are unobscured by other structures.
Douglas Corporation has made its CAM system available for this project, which would be no more difficult than designing and making molds for aircraft parts, an everyday occurrence at the company's plant in St. Louis.

Even better than the manufacture of prostheses would be the prevention of wrist damage. Such a project is of great interest to Weeks, head of the Milliken Hand Clinic at Barnes, who sees many patients with occupational wrist injuries. "Any machine that vibrates creates a significant amount of stress that is absorbed and transmitted into the wrist area," says Weeks. "A person who uses a machine such as an air drill can develop Kienböck's disease, which is painful and eventually limits motion. Such people can actually end up with a total fusion of the wrist bones and, once they have that, they become unable to do many jobs."

Persons prone to Kienböck's disease may start out with unusual wrist mechanics. Therefore, a computer program assessing wrist mechanics could screen persons at risk if they work with vibrating machinery. However, such a project would be possible only after wrist mechanics are better understood.

As well as reducing the incidence of Kienböck's disease, the computer may help patients who already have the disease. "One method of management," says Weeks, "is to fuse certain of the wrist bones to distribute the load better. Using the computer, we would like to be able to predict what would happen if the bones were fused."

Patients with fractures might also benefit from computer intervention. "Imagine someone falls and fractures the radius," muses Weeks, "tilting his wrist out of position. Therefore the wrist bones are subjected to completely different stresses than normal. Using the CAD/CAM system, we would determine what the stresses are under those circumstances and what we would have to do to correct them back to a point where the patient no longer has pain in the wrist."

Logan predicts that surgeons will also find the three-dimensional images helpful. "The advantage of having a pre-operative three-dimensional picture is the problem can be seen before an incision is made," he says. "And since surgeons work in a three-dimensional world, it helps to see things in three dimensions. Not every wrist problem requires three-dimensional imaging. But for complex problems, I think it's one more arrow in our quiver. For these difficult situations, three-dimensional imaging has a definite advantage over plane x-rays and two-dimensional CAT scans.

"What impresses me," says Logan, "is that the technology is going by leaps and bounds. We just have to find ways of applying it. We are limited only by our imaginations."

Linda Sage, Ph.D. (biochemistry), is a freelance writer.

---

**No-Slip Hip**

Correct fit of the cementless hip prosthesis becomes crucial, since the device is not glued into place. Wayne Daum, M.D., assistant professor of orthopedics, is collaborating with Michael Vannier, M.D., to insure that the metal and bone make an absolutely tight fit. To do this, Vannier writes computer software that electronically matches the dimensions of a patient's thigh bone and pelvis with those of available prostheses. (Currently, the device is manufactured only in a limited number of sizes.) The computer matches the patient's thigh bone with the best-fitting prosthesis. Eventually, the technology may be extended by machining a prosthesis to the exact dimensions of individual patients.

In addition, the computer is also a valuable tool for patients requiring procedures other than total hip replacement. For example, some patients with avascular necrosis (blockage of blood flow to the head of the thigh bone) require an osteotomy—reshaping contours of diseased areas of the bone. "Vannier has helped me," says Daum, "by performing CAT scans on a patient so that the bone's three dimensions can be projected. This helps me know exactly how and where I would make a cut, or if it's even feasible to change the anatomy of the hip joint in order to alleviate symptoms."

"The single most important event that has occurred in the past 20 years in the treatment of arthritis has been the development of these new technologies," says Floyd Pennington, Ph.D., of the Arthritis Foundation, headquartered in Atlanta. "More and more people will be helped in the future."
First-Year Slice of Life

Medicine is “a lifestyle, not just a job,” for Karen Scharenberg, first-year student at the School of Medicine. “Knowing that, it took me a while to decide to commit to that as a career. I didn’t want to take a place from someone else in medical school unless I was sure I’d use those skills.”

But in working towards that career, she playfully describes her first year as including “many ‘ology’ classes,” such as cell biology. Although serious about her career, she realizes the hazards that can come from slavish devotion to her studies.

She strives to establish a healthy balance among school, exercise, and social life. Among her hobbies are running, lifting weights three times a week, as well as ice skating at Steinberg Rink in Forest Park.

“I’m careful not to let myself feel guilty about the time I spend relaxing,” says Scharenberg. “The study habits I develop now are what will carry me through the rest of school and training. Medicine can’t be my entire life. Those extra 10 hours a week I might spend studying could earn me higher grades, but for me, it’s more important to spend that time some other way, like exercising.

But everyone in medical school knows how to drive themselves — we all had to do it to get where we are today.”
Karen Scharenberg, shown here with former HEW Secretary Juanita Kreps, is an Olin Fellow. Kreps came to the university last fall as speaker for the Tenth Annual Olin Lecture. Left Scharenberg and fellow student Thomas Kim spend a great many hours in small group study sessions, a traditional part of the life of any medical student. Bottom Scharenberg and Laura Dyer were lab partners in anatomy, another traditional area of study for a first-year student. Outside anatomy lab, Scharenberg and Dyer team up as roommates.
Right Roy R. Peterson, Ph.D., professor of anatomy and neurobiology, is a fixture for first-year students who spend at least nine hours each week working with him and learning from him in their human anatomy course. Below Karen and her brother Andy find a rare moment to enjoy a St. Louis restaurant. Andy, 20, is a senior majoring in biochemistry at Indiana University, his sister's alma mater. Like his sister, who earned the B.A. in chemistry, he hopes to be a medical student next fall. Far right Scharenberg spends a good portion of her time in a time-honored tradition for first-year students: solitary study.
Innovations in medical computer imaging, discussed in this issue of Outlook, hold great promise for primary care physicians. The powerful electronic devices used to visualize human organs and study molecular structure can be modified to communicate information stored in traditional medical records. Indeed, managing the ever-growing flow of medical information within a complex medical care system presents one of our greatest challenges.

Consider, for example, how policy changes by government and private industry have altered the hospital's role. Prospective payment schemes and pre-admission screening programs have appropriately emphasized the importance of performing more diagnostic and therapeutic procedures in less expensive ambulatory care settings, whenever possible. These new regulatory efforts recognize that until recently, patients who were not acutely ill were often hospitalized solely to expedite diagnosis.

Aside from the expense, hospitalization for diagnosis was generally beneficial. It was convenient for the patient, and it centralized the collection and processing of medical information. The primary care physician provided a medical history that included principal diagnoses, current medications, and results of past medical interventions. Complete medical records minimized redundant medical tests. And interactions between prescribed drugs were more easily prevented by meticulous record-keeping.

Dramatic changes in our country's health care policy have virtually eliminated this use of the hospital. This has created a decentralized system for medical diagnosis and treatment. Extensive diagnostic programs, once performed conveniently in the hospital, will now be conducted in a number of different facilities often separated by appreciable distances. Patients with complex medical problems will spend more time traveling between physicians' offices. Patient specimens will be shipped to remote laboratories for analysis. Expensive technologies — digital angiography, magnetic resonance imaging and positron emission tomography (PET) — will become outpatient services. The primary care provider, responsible for coordinating all aspects of patient management, must find new ways to gather and analyze medical information obtained from these disparate sources.

Computing facilities can manipulate, transmit, and display high-resolution medical images. These technologies can also communicate physical findings, laboratory data, and consultation notes. Thus, the same computer that displays a patient's chest X-ray can transmit crucial information about drug allergies, past diagnoses, and recent laboratory tests. This can be done in pictorial format quite unlike the sterile video screen to which we have become accustomed. Graphic display of laboratory tests, for example, may result in earlier detection of important clinical trends. Rural physicians could send X-rays, electrocardiograms, medical notes, and photographs to urban specialists, thus sparing patients from trips to a major medical center. In the future, computers may help physicians by suggesting diagnoses and recommending therapy.

Over the last century, medical technology has occasionally been applied thoughtlessly and indiscriminately. Like other technologies, medical computer imaging offers promise and peril: it could help solve a pressing need in medicine, but it could also be misapplied and abused. Used properly, computers could facilitate communications, enhance medical care, decrease costs, and improve medical education. Used improperly, computers could destroy privacy, dehumanize care, increase costs, and promulgate damaging misinformation. At this juncture, our challenge is to use this powerful new technology wisely.

Mark E. Frisse, M.D. '78
Assistant professor of medicine
Washington University School of Medicine

This is the opinion of the author, not necessarily shared by Washington University, Washington University School of Medicine, Washington University Medical Center, or the policy of any of these entities. Outlook welcomes replies to this editorial and invites contributions from its readers on other subjects.
**Kroc Foundation Establishes Research Chair**

By a gift of $1 million, The Kroc Foundation of Santa Barbara, Calif., has established a chair to support biomedical research in diabetes and endocrine diseases at the School of Medicine.

The late Ray A. Kroc, founder of McDonald's Corporation, was a creator and sole benefactor of The Kroc Foundation. The endowment is named for his brother, Dr. Robert Kroc, in recognition of his accomplishments as a university teacher, pharmaceutical researcher, and developer of the Kroc Foundation's research grants and conferences programs.

Establishment of The Robert L. Kroc Chair in Diabetes and Endocrine Diseases was announced Jan. 9 during a luncheon at the medical center. Guests of the university included Dr. and Mrs. Robert Kroc, as well as Fred L. Turner, Chairman of McDonald's Corporation and a member of the Foundation's Board of Directors.

The first Robert L. Kroc Professor will be Paul E. Lacy, M.D., Ph.D., former head of the Department of Pathology. Lacy, department head for more than 20 years, stepped down from that position earlier this year to concentrate full time on research. One of his most important achievements is success in controlling diabetes by transplanting islets of Langerhans, clusters of insulin-producing pancreas cells.

Lacy commented upon a key source of his research support: "The success of our research program on islet transplantation can be attributed to the faith, trust and financial support that has been provided to us by the Kroc Foundation for many years. This critical support has made it possible for us to bring islet transplantation to the threshold of human application."

The Kroc Professorship in diabetes and endocrine diseases is the first of three research chairs to be established by the Kroc Foundation. Since 1969, the foundation has provided research support totaling more than $46 million to University has received Kroc Foundation grants totaling about $2.5 million. The first grant was given in 1971 to start Lacy's work in transplanting islets of Langerhans. A total of 15 grants have been made for research relating to diabetes as well as multiple sclerosis, various forms of arthritis, and connective tissue and bone disease. Thirteen principal investigator's have directed this research. Many of these scientists and others from Washington University participated in Kroc Foundation research conferences at its headquarters at Ray Kroc's ranch in the Santa Ynez Valley of California.

Lacy, a native of Trinway, Ohio, earned the doctor of medicine degree cum laude in 1948 from Ohio State University, and the doctor of philosophy degree in pathology in 1955 from the Mayo Foundation of the University of Minnesota. He interned at White Cross Hospital in Columbus, Ohio, and served a fellowship in pathology at the Mayo Clinic. He joined the Department of Anatomy at Washington University in 1955.

**Corporations Support ALLIANCE**

Avon Products Foundation and the Mallinckrodt Fund have pledged $750,000 to the ALLIANCE FOR WASHINGTON UNIVERSITY, a $300 million fund-raising campaign announced last year. Mercantile Bancorporation, Inc., has made a $400,000 gift to the ALLIANCE. Announcements of both corporate gifts was made by William H. Danforth, Chancellor of Washington University.

The Avon/Mallinckrodt pledge earmarks $370,000 for the Clinical Sciences Research Building (CSRB) at the School of Medicine. Mercantile Bancorporation's gift will be divided, with $200,000 used toward the CSRB.

The recently dedicated 382,080-square-foot CSRB is the central link joining the School of Medicine, through a series of enclosed pedestrian bridges, with Barnes, Jewish, and Children's hospitals. The CSRB accommodates research facilities and offices for six clinical departments: anesthesiology, medicine, psychiatry, pathology, radiology and surgery.
Virginia V. Weldon, M.D., deputy vice chancellor of the School of Medicine, has been named chairman-elect of the assembly of the Association of American Medical Colleges (AAMC).

Her election to the post, announced last fall during the annual meeting in Chicago, marks the first time in the AAMC's 108-year history that a woman has been chosen to lead the association. Weldon will serve as chairman beginning in the fall of 1985.

With a membership of more than 100,000, the AAMC represents the entire community of academic medicine, including 127 medical schools, 430 teaching hospitals and over 70 biomedical societies. The Washington, D.C.-based association is a leader in developing programs to advance medical education, biomedical research and health services in the United States.

Weldon has been a representative to the AAMC's Council of Academic Societies since 1976, serving in 1984 as the council's chairman-elect. She is recognized nationally as a spokesperson on issues in medical education and biomedical research, and on legislation affecting health care, especially its costs. A specialist in pediatric endocrinology, she is well known for her studies of mechanisms of abnormal growth in childhood.

Weldon is vice president of the Washington University Medical Center and professor of pediatrics at the School of Medicine. She also is on staff at Barnes and Children's hospitals. She came to the university in 1968 as an instructor, and was named professor of pediatrics in 1979.

She earned the doctor of medicine degree from the University of Buffalo School of Medicine and the bachelor's degree from Smith College. Weldon was an intern and assistant resident in pediatrics at The Johns Hopkins Hospital in Baltimore, and later held a fellowship and instructorship at Johns Hopkins Medical School.

Her professional memberships include the Institute of Medicine of the National Academy of Science, Endocrine Society, and the Society for Pediatric Research. She is a fellow of the American Association for the Advancement of Science. Weldon has received a number of awards and honors, and has published many journal articles on pediatric endocrinology.

Child Guidance Center at Children's Hospital

Two separate services have combined operations to create the new Child Guidance Center, located in Children's Hospital at 400 S. Kingshighway Blvd.

The new center was formed when the Child Guidance Clinic moved to Children's Hospital and expanded its program, joining with the outpatient psychiatry service already in existence at the hospital.

"The move to Children's Hospital places the center, for the first time, directly in the medical school environment," said Felton Earls, M.D., director and Blanche F. Ittleson Professor of the William Greenleaf Eliot Division of Child Psychiatry. "Working in that environment will increase communication between pediatricians and psychiatrists. Also, training of these physicians will improve, along with the mental health care of children." Earls is a physician at Barnes, Children's and Jewish hospitals.

The Child Guidance Center is under the medical direction of Haruo Kusama, M.D., assistant professor of clinical child psychiatry at the School of Medicine. It functions as a general outpatient psychiatric program for Children's Hospital, and has developed a strong link with the hospital's inpatient unit, directed by assistant professor of child psychiatry Zila Welner, M.D. Both Kusama and Welner are physicians at Barnes and Children's hospitals.

Patients are easily referred to the inpatient unit, and upon discharge are often referred to the guidance center for follow-up treatment.

The center treats children from infancy through 18 years of age using a multidisciplinary approach that combines psychiatry, psychology and social work services. The staff offers special treatment for sex abuse/incest, depression, hyperactivity and other developmental and behavioral problems. The center provides consultation to area schools, and staff members also conduct in-service training sessions for guidance counselors in the St. Louis public schools.

The Child Guidance Center, a United Way agency, bases its fees on a sliding scale. Earls noted that although 25 percent of the center's patients come from families with incomes above $30,000, 30 percent pay $2 an hour or less.

To make appointments, or for further information, call the Child Guidance Center at 314-454-6201.
EB Center Receives Gifts

The epidermolysis bullosa center at the School of Medicine has received a $20,000 gift from the McDonnell Douglas Employee Charity and Community Services Board. McDonnell Douglas employees presented the contribution as support for research at the St. Louis center, one of few sites in the nation to study epidermolysis bullosa (EB).

The center also recently received a $4,500 contribution from the Veterans of Foreign Wars Hall in St. Charles. The VFW gift to support research was given in the name of EB patient Jamie Miller, an eight-month-old boy whose father is a member of the St. Charles post.

A rare genetic skin disorder, EB is also known as the "thin skin disease" because of the blistering, scarring and destruction of the skin and mucous membranes that it causes. There is very little treatment and no known cure for the disease. In America alone, 14 varieties of EB threaten the lives of 25,000–50,000 patients, mostly children.

The Washington University center was established in 1983 with a $25,000 donation from the Dystrophic Epidermolysis Bullosa Research Association. Since then, it has also received a gift from the Jamie Hoke Living Trust Fund in Pennsylvania. Locally, the Epidermolysis Bullosa Foundation is working to raise $1 million to create an operating endowment for the center.

Eugene A. Bauer, M.D., director, and center researchers are trying to determine causes of various forms of EB, and hope eventually to develop a cure or more effective treatment for the disease. Bauer is professor of dermatology at the School of Medicine and a physician at Barnes, Children's and Jewish hospitals. More information is available through the EB center at 314-362-2304.

Raichle Receives Poiley Award

Marcus E. Raichle, M.D., professor of neurology and radiology, has received the Sarah L. Poiley Memorial Award from the New York Academy of Sciences.

The award was presented last winter during the academy's 167th annual meeting in New York City. Raichle, who was cited for his work in applying quantitative radiotracers techniques to the study of the human brain, shares the award with Michael E. Phelps, M.D., of the University of California–Los Angeles.

Raichle is also professor of biomedical engineering at Washington University, and a staff physician at Barnes, Children's and Jewish hospitals.

Raichle is noted for applying positron emission tomography — PET scanning — to study the human brain. His work has included studies of the normal brain and its response to a variety of stimuli, evaluation of patients at risk for stroke, an analysis of certain chemical receptors in the brain, and investigations of the origin and physiology of seizure disorders.

One of his most recent studies involved PET examinations of persons struck with panic disorder, which is characterized by recurrent, spontaneous attacks of severe anxiety. Raichle and other Washington University researchers, including Eli Robins, M.D., Wallace Reardon Professor of Psychiatry, were the first to identify a biological basis for panic disorder, as described in "When Fear Strikes" (page 12).

Raichle joined the faculty in 1971 as a research instructor in neurology. He received the doctor of medicine degree in 1964 from the University of Washington School of Medicine, and received his training in neurology and his introduction to neurological research at the Cornell University Medical Center in New York City.

Raichle is on the editorial board of Annals of Neurology, Brain, and the Journal of Cerebral Blood Flow and Metabolism, and is a former study section member and frequent advisor to the National Institutes of Health.

He is a member of many professional societies, among them the American Academy of Neurology, the American Neurological Association, the International Society of Cerebral Blood Flow and Metabolism, the American Physiological Society and the Society for Neuroscience.

J. Regan Thomas, M.D.

Thomas Elected to National Posts

Regan Thomas, M.D., assistant professor of otolaryngology, has been elected to posts with two national medical associations. Thomas has been named a member of the board of directors and education chairman of the American Academy of Facial Plastic andReconstructive Surgery, Inc. He also has been appointed to the American Medical Association's Committee on the Young Physician — a new seven-member committee that will address the needs of physicians under age 40.

Thomas is on staff at Barnes and Jewish hospitals. Before joining the Washington University faculty in 1983, he was clinical assistant professor of otolaryngological surgery at the University of Missouri Medical Center.

He received the doctor of medicine degree from the University of Missouri School of Medicine in 1972. Thomas trained in surgery at Yale University and in otolaryngology at the University of Missouri School of Medicine.
Sobel Receives Distinguished Achievement Award

Burton Sobel, M.D., professor of medicine and director of the cardiovascular division at the School of Medicine, received the 1984 Distinguished Achievement Award from the American Heart Association (AHA). Sobel is one of six recipients of the award, presented last fall during the AHA’s Scientific Sessions in Miami Beach, Fla.

The Distinguished Achievement Award recognizes individuals for major contributions while serving on AHA scientific councils, for adding substantially to new knowledge in the field or to teaching and clinical care, or for leadership in professional organizations.

Sobel, a fellow of the AHA’s Councils on Clinical Cardiology and Circulation, is internationally renowned for his thrombolytic therapy research. Last year, he published results of a pilot study using an experimental chemical called t-PA, tissue plasminogen activator. In six out of seven patients, t-PA quickly and safely stopped a heart attack in progress by dissolving the blood clot blocking a coronary artery. The new therapy could ultimately save thousands of lives each year.

Sobel is director of a Specialized Center of Research (SCOR) which has received renewed funding of $9.2 million for the next five years from the National Heart, Lung and Blood Institute. The research, which involves 40 investigators from 12 departments, deals with the heart’s response to ischemic injury and is designed to identify new therapeutic approaches for heart disease.

Sobel joined Washington University in 1973 as an associate professor of medicine and director of the cardiovascular division. He was named professor in 1975, and has served as adjunct professor of chemistry since 1979. He also serves as chief of cardiology at Barnes Hospital.

Sobel received the doctor of medicine degree magna cum laude from Harvard Medical School. He served an internship and residencies in medicine at Peter Bent Brigham Hospital, and was an assistant in medicine at Harvard Medical School.

A member of many professional societies, Sobel also serves on a number of research advisory committees and editorial boards. He is presently editor of Circulation. He is the recipient of the 1971 National Heart and Lung Institute’s Career Development Award, and the 1981 Heart Research Foundation’s International Award.

Sobel has lectured nationally and internationally, and has written more than 300 articles on his cardiology research.

Owens Elected to American Board of Anesthesiology

William D. Owens, M.D., has been elected to serve a four-year term on the board of directors of the American Board of Anesthesiology. Owens is professor and head of the Department of Anesthesiology.

The American Board of Anesthesiology is the certifying body for anesthesiologists in the United States. Only 12 individuals are elected to its board of directors.

Owens was appointed head of the anesthesiology department last January, after serving as acting head of the department for more than two years. He joined the School of Medicine faculty in 1973 as an assistant professor of anesthesiology, and was named professor in 1981 and acting head of the department in 1982.

Owens is anesthesiologist-in-chief at Barnes and Children's hospitals. He also serves as medical director of respiratory therapy and co-director of the surgical intensive care unit at Barnes Hospital.

He received the doctor of medicine degree from the University of Michigan in 1965, and interned at the Presbyterian Medical Center in Denver, Colo. Owens served a residency in the Department of Anesthesiology at Massachusetts General Hospital in Boston, and a fellowship in the Department of Anesthesiology at Harvard Medical School.

He is a fellow of the American College of Anesthesiologists and a member of numerous other professional organizations. A principal investigator of various anesthesia research projects, Owens has been an invited lecturer and visiting professor, and has delivered scientific presentations at universities and organizations throughout the United States and Canada. He is associate editor of Survey of Anesthesiology and has written more than 40 journal articles.
Lipid Research Center researchers seek persons with high blood pressure for research on new anti-hypertensive medicine. The Lipid Research Center is part of the Department of Preventive Medicine at the university.

Study participants must be between the ages of 18 and 75, and have no other significant illnesses. Persons already taking medication for high blood pressure can be accepted if their private physicians agree to stop medication for three to four months. The study lasts about 14 weeks. After an initial screening period, participants will receive a complete physical examination, electrocardiogram, blood count and blood cholesterol. Results will be made available to the participant's private physician.

For more information, contact the Lipid Research Center from 8 a.m.–3 p.m. weekdays, telephone 314-362-3500.

Morton F. Arnsdorf, M.D., professor of medicine and chief of cardiology at the University of Chicago's Pritzker School of Medicine, delivered the first Rudolph A. Tuteur Lecture. Arnsdorf's lecture was titled "On the Nature of Academic Medicine: Its Art, Science and Business."

The lectureship is endowed by family, friends and colleagues of the Tuteur family in memory of Rudolph A. Tuteur, to promote understanding of problems in caring for the chronically ill. The elder Tuteur suffered from chronic obstructive pulmonary disease. His son, Peter G. Tuteur, M.D., is associate professor of medicine at the School of Medicine and a staff physician at Barnes Hospital.

Arnsdorf's research concentrates on the electropharmacologic actions of antirhythmic drugs on the cardiac conduction system. He also helped study his academic health center's relationship to the community while a member of the Patient Affairs Committee, and served as chairman of his school's Marketing, Referral and Information Task Force.

Arnsdorf received the bachelor of arts degree from Harvard University and the doctor of medicine degree from Columbia University. He completed postgraduate training at the University of Chicago Hospitals and Clinics and at Columbia-Presbyterian Medical Center. He is a member of many medical societies, serves on the editorial board of professional journals and is author of more than 40 articles and book chapters.

C. Ronald Kahn, M.D., noted diabetes researcher, recently delivered the 12th annual Carl V. Moore Memorial Lecture. Kahn is professor of medicine at Harvard Medical School and research director of the Joslin Diabetes Center in Boston. Title of the lecture was "The Insulin Receptor as an Insulin Sensitive Enzyme: Biochemical Implications."

The Moore Lecture is sponsored each year by the Department of Medicine at Washington University in honor of the late Carl V. Moore, M.D. Moore was Busch Professor and head of the Department of Medicine, first vice chancellor for medical affairs at the School of Medicine, and president of the medical center. He died in 1972.

Kahn investigates insulin receptors and insulin action, insulin-like growth factors, diabetes mellitus, hypoglycemia, and immunity and autoimmunity in endocrine disorders.

A faculty member at Harvard Medical School since 1981, he is chief of the Division of Diabetes and Metabolism at Brigham and Women's Hospital and a staff physician at the New England Deaconess Hospital. Kahn was also on the faculty at the University of Health Sciences in Bethesda, Md., and George Washington University, and was chief of the Diabetes Branch Section on Cellular and Molecular Physiology at the National Institute of Arthritis, Metabolism and Digestive Diseases.

He earned the doctor of medicine degree from the University of Louisville, and completed an internship and residency in medicine at Barnes Hospital. He also trained with the Clinical Endocrinology Branch of the National Institute of Arthritis, Metabolism and Digestive Diseases.

Kahn serves on committees for many national organizations, including the National Diabetes Board, the American Diabetes Association and the Juvenile Diabetes Foundation. Among his honors are awards for his research from the Juvenile Diabetes Foundation, the American Diabetes Association and the American Federation for Clinical Research.

Kahn has written more than 140 reports on his research, as well as over 65 reviews, chapters and editorials. He is frequently invited to lecture nationally and internationally on his research.

Sol Sherry, M.D., dean and distinguished professor of medicine at Temple University School of Medicine in New York City, delivered the second annual Edward Massie Lecture in Cardiovascular Disease. Sherry, former professor and co-chairman of the Department of Medicine at Washington University School of Medicine, discussed "Washington University and the Development of Thrombolytic Therapy." The lecture is sponsored by the division of cardiology to honor Edward Massie, M.D., professor emeritus of clinical medicine at Washington University.

Sherry is considered a pioneer in understanding the thrombolytic system and its use in patients. He was responsible for the first extensive purification of tissue plasminogen activator. As early as 1950, Sherry studied streptokinase, an enzyme extracted from streptococcus bacteria that is now the most widely used clot-dissolving agent. He was instrumental in proving that streptokinase can be effective in opening blocked blood vessels in humans.

Sherry was a faculty member at Washington University School of Medicine.
from 1954 until 1967, when he became chairman and professor of the Department of Internal Medicine at Temple University. He has also served as director and director emeritus of the Specialized Center for Thrombosis Research at Temple University. Earlier in his career, Sherry served on the faculty at New York University School of Medicine and at the University of Cincinnati College of Medicine.

He is currently physician-in-chief at Temple University Hospital and consultant in medicine at Germantown Hospital. While in St. Louis, he was on staff at Jewish Hospital, where he was director of the Division of Medical Services, and at Barnes Hospital.

Dorothy T. Krieger, M.D., D.Sc., professor of medicine and director of the division of endocrinology at Mount Sinai Medical Center in New York, delivered the ninth annual Mildred Trotter Lecture.

The Medical Alumni Association has honored Mildred Trotter by endowing a lectureship in her name. Trotter, professor emerita and lecturer in anatomy since 1967, is the first female faculty member to be recognized in this way. In recognition of Trotter's deep concern for the role of women in academic life, the lectureship is being used to bring a distinguished female scientist to the University every year.

Combining clinical responsibilities and laboratory investigation, Krieger has developed special expertise in the treatment of Cushing's disease. She researched hypothalamic-pituitary-adrenal relationships, studying the factors influencing the circadian periodicity of adrenocorticotropic hormone (ACTH) and corticosteroids. Her work expanded to include the study of other brain peptides, such as beta-lipotropin and beta-endorphin, which, along with ACTH, derive from a common precursor molecule. Brain peptides occur in tissues other than the brain as well as in unicellular organisms. Their role as neurotransmitters or neuromodulators and their evolutionary origin and significance has been recently discussed by Krieger in a Science review, "Brain Peptides: What, Where, and Why?".

Krieger has written numerous scientific papers and edited several books. Her book, Cushing's Syndrome, was published in 1982. Together with M.J. Brownstein and J.B. Martin, she was coeditor of Brain Peptides, published in 1983.

Krieger received the M.D. from Columbia University College of Physicians and Surgeons after graduating summa cum laude from Barnard College. She serves on the National Advisory Council on Aging (NIH), was named to the Society for Experimental Biology and Medicine, and is a Fellow of the New York Academy of Sciences. She has been active in a number of national and international committees and has served on the editorial boards of a number of journals. Krieger is a Fellow of the American Board of Internal Medicine.

Steven J. Rose, Ph.D., director of the Program in Physical Therapy, has been appointed to a special commission of the American Physical Therapy Association (APTA).

Rose will serve on the APTA President's Commission on University Relations, which was formed to promote physical therapy training in higher education. Members of the commission identify ways the association can improve communication with universities, assist in developing master's degree programs in physical therapy, and consider ways to strengthen physical therapy as a discipline within the allied health care field.

Under Rose's direction, Washington University has established a model program that allows practicing physical therapists to pursue master's degrees by combining clinical practice with research.

Rose also serves as co-director of the Department of Physical Therapy at the Irene Walter Johnson Rehabilitation Institute.

Infair '84, an overview of databases, computer hardware and information networks at the medical center, was sponsored by the medical library recently. The Infair, the first of annually-planned events, included demonstrations and mini-seminars, plus exhibits by software and hardware vendors.

And the Winners Are . . .

The annual awards luncheon for first-, second-, and third-year classes in 1983-84 was held recently. Dean Herweg announced the award winners. The prizes, and the recipients, are:


The Edmund V. Cowdry Prize in Histology, awarded to Jesse S. Little, Jr.

The Dr. James L. O'Leary Neuroscience Prize, awarded to Robert M. Forstot.

The Carl F. and Gerty T. Cori Prizes in Biochemistry, awarded to Roger C. Inhorn.

The Antonette Frances Dames Prize in Physiology and Biophysics, awarded to Grant W. Rogero and Edwin K. Silverman.

The Howard A. McCordock Book Prize in Pathology, awarded to Nancy L. Bartlett.

The Dr. Margaret G. Smith Award, given to Judith L. Zier.

The Medical Center Alumni Scholarship Fund Prize, awarded to Anthony C. Pearlstone and Regina M. Resta.

The Academic Achievement Award, given to Patrick B. Sandiford.

Oliver H. Lowry Prize in Pharmacology, awarded to Michael Apkon.

The Richard S. Brooking Medical School Prizes, awarded to Dwight A. Towler, Charalabos S. Chrysikopoulos, and Diane R. Levisohn.

The Dr. Robert Carter Medical School Prizes, awarded to Peter L. Smith, Steven M. Cohn, and Sharon E. Coplen.
The Florence Nightingale Pledge, recited at the capping ceremony for nurses, says in part: "... With loyalty will I endeavor to aid the physician in his work..." Graduates of the School of Nursing when it was a part of the university have held true to their pledge. A gift of $35,000 — the funds remaining in the nursing school's alumni association treasury, plus a generous donation by Miss Hazel Duncan to round up the sum to that figure — has established a research fund. This endowment, named the Washington University School of Nursing Alumni Association Research Fund, supports clinical research projects selected by the medical school.

But the decision to donate these funds was not made lightly. A seven-member committee, chaired by Ella Mae Hott Magness, sent more than 1,300 ballots to nursing alumnae, asking their opinions on the disposition of this money. Of the 789 who responded, an overwhelming majority chose to donate the funds to the School of Medicine, establishing an endowed fund named for the alumni association.

Originally established in the early 1920s, the School of Nursing Alumni Association was set up to endow a bed for nurses at Barnes Hospital, says Josephine Glen-dinning Heys, '22. "We scraped together whatever we could from luncheons, bake sales — you name it, we did it," remembers Heys. "But it wasn't enough money. So we asked alumnae for donations."

Over the years, the money lay dormant. It wasn't until the 50th reunion of the class of '25 that anyone seemed interested in tracking down the whereabouts of the money and deciding on its disposition. Evelyn Peuser Aivazian, '25, now residing in Hanford, Calif., gave Heys an ultimatum: "I expect you to have done something with that endowment fund by the time I come back for my 60th class reunion [in 1985]."

Heys accepted the challenge, and in the summer of 1984, met with Magness, Duncan, and fellow alumnae Theda Guzman, Ella Brace Lange, Virginia Kleissle Macnish, and Mildred Pemberton. They, along with Jack Stiefkas (director of medical alumni and development programs) and Chris Owens (director of medical alumni programs), decided to poll alumnae about their wishes concerning the disposition of these monies. The rest, as they say, is history.

"Endowment funds for research are crucial to our work," remarks M. Kenton King, M.D., Dean of the School of Medicine. "They provide flexibility to pursue new ideas, and they support bright young scientists who want to develop careers in medical research. We appreciate the generous spirit of all nursing alumnae who made this endowment gift possible."

From left: Josephine G. Heys, Ella M. Magness, and Hazel B. Duncan, members of a seven-member committee to establish the School of Nursing Alumni Association Research Fund.

Medical Center Alumni Association
Box 8049
660 S. Euclid
St. Louis, MO 63110

David T. Hammond, M.D. '60
President
Jack Stiefkas, Director
Medical Alumni and Development Programs
Chris Owens, Director
Medical Alumni Programs
Ruth Moenster
Secretary
It is March 1978. Two physicians drive through Forest Park on their way to work at Barnes Hospital in St. Louis. Amid the rush-hour traffic, they spot a jogger who collapses. Both race to administer cardiopulmonary resuscitation. The jogger revives, and he is so grateful for CPR's "miracle" that he later becomes an active proponent of the technique.

One of the Good Samaritans is Gerald T. Perkoff, M.D. '48, now at the University of Missouri (Columbia). The other is Richard D. Aach, M.D. '59. Why did Aach go to the jogger's aid — in our litigious society, wasn't he afraid of a malpractice suit? "That thought never entered my mind," he says. "I just saw a person who needed help, and frankly, as a physician, I felt compelled to respond."

Richard Aach has always approached his profession with a sense of purpose. In 1961, after the St. Louis native completed his residency, he entered the Epidemic Intelligence Service at the Centers for Disease Control (CDC) in Atlanta. Explains Aach: "I was fascinated by the idea that if an epidemic occurred, I could investigate the problem and apply epidemiologic techniques to determine how it is spread and how it could be controlled. I also saw that by doing that, you could reach and care for the medical needs of large numbers of people, as opposed to a private practice where one is in contact with fewer people."

The years at CDC proved pivotal. Assigned to the hepatitis unit of the surveillance branch, Aach traveled the country investigating outbreaks of hepatitis. In August 1961, a two-week stay among the Tlingit Indians of Alaska, in the remote fishing village of Hoonah, focused his attention on hepatitis: "Hepatitis occurs naturally there, and I was living with the disease rather than just seeing sporadic cases in a hospital."

It wasn't until later that Baruch Blumberg, M.D., then at the Institute of Cancer Research in Philadelphia, discovered the Australia antigen, which would become the missing link in the epidemiologic characterization of one of the two known forms of hepatitis. Until 1968, when Blumberg and Alfred M. Prince, M.D., of the New York Blood Center identified the antigen's link with serum hepatitis, as it was then called, the disease could only be diagnosed by clinical impression and general laboratory tests. Once the Australia antigen was identified, it became possible to make a specific serologic diagnosis of hepatitis B.
In 1964, Aach returned to Washington University as chief resident in medicine after a two-year stint at CDC and a year as a fellow in liver diseases at Yale University. Later, in collaboration with Charles W. Parker, M.D., now professor of medicine and microbiology and immunology, and Joseph W. Grisham, M.D., he published a number of studies on the immunologic aspects of liver disease.

In 1970, they developed a radioimmunoassay test, one of the first sensitive techniques for screening carriers of hepatitis B. To test for the disease, they used radioactive isotopes to label antibody against purified Australia antigen. They added this to serum samples to be screened, and used a gamma counter to detect any Australia antigen in the antigen-antibody reactions.

"At the time," he observes, "a test for Australia antigen was a major contribution because it added to the pool of information about hepatitis, its manner of spread, its complications, and its prevention. But it was not unique. A number of tests have come along subsequently that are just as good, if not better. However, at the time, it was extremely exciting."

Excitement is a word that constantly punctuates Aach's speech. As he describes momentous events in his career, or recounts the major breakthroughs in his field, the enthusiasm with which he speaks approximates his experience.

He focused most of his research on post-transfusion hepatitis, because in the United States, blood transfusions were (and still are) the most common means of transmitting viral hepatitis. During the '70s, with funding from the National Institutes of Health, he headed a research team in St. Louis — one of five nationwide that comprised the Transfusion-Transmitted Viruses Study Group. From 1974 to 1979, the team studied approximately 1,500 patients (about 10 percent of whom had hepatitis) before and after they received transfusions. And in looking at a cross section of the United States, a massive amount of information was compiled: the rate of hepatitis, its manner of transmission, clinical patterns, and prevention. As the only study to compare rates of hepatitis among patients who were transfused with the rate among a nontransfused control group, the project amassed data that had not been gathered before.

Aach likens this period of intellectual ferment to the explosiveness of polio research in the '50s and early '60s. "It was a marvelous era of being able to recognize, first, hepatitis B and then hepatitis A," he reminisces. "So we've come from the late '60s when we could epidemiologically characterize hepatitis and diagnose it only by impression, to the present, when we have substantially improved diagnostic tests. By using better immunological techniques, for example, we have developed good tests for hepatitis A and B. We have also developed better vaccines for hepatitis B, and on the horizon are newer vaccines that will be synthesized by molecular hybridization, or even synthetic vaccines which are made right in the test tube. Now, a few trials are underway for a hepatitis A vaccine. So, it has really been a very exciting decade."

It was also a time of frustration. As frequently happens in research, finding one set of answers raised new questions. As a result of their work on transfusion-associated hepatitis, in 1974 researchers discovered another form of the disease. "Non-A, non-B hepatitis," Aach concedes, "is a source of frustration to clinicians and researchers because at this point, we cannot identify the agent or agents responsible for it."

"Non-A, non-B hepatitis accounts for about 90 percent of post-transfusion hepatitis. About 250,000 new cases of hepatitis occur in the U.S. each year as a result. It is now being intensely investigated, but after 10 years, it is still a diagnosis of exclusion. Consequently, we have no means of preventing its occurrence from blood transfusions, for example."

Recent work by researchers in the U.S. and Sweden has been cited as evidence that an unusual type of virus (a retrovirus) may be the culprit behind non-A, non-B hepatitis. If followup work confirms these preliminary findings, then a specific screening test — and a vaccine — may be developed. Eventually, transfusion-associated hepatitis may be cited only as an entry in the history of medicine.

However, Aach's research has been set aside to allow time for other interests. Since 1980, he has been physician-in-chief and head of the department of medicine at Sinai Hospital in Baltimore, and professor of medicine at The Johns Hopkins University. Thus, at the moment, he is primarily involved in program development. During his tenure, the number of applicants to the program has quadrupled, and the academic staff has grown substantially.

Yet someone who has been at the forefront of research in his field for a decade does not easily relinquish his scholarly pursuits. Aach still attends national and international meetings, where he is often invited to lecture on hepatitis. But, as he says in a somewhat wistful tone: "I'm not as actively involved in research as I would like to be. Because of various priorities, that was the one that temporarily had to give way."

The journals' loss is his students' gain, because Aach (named Teacher of the Year in 1974 at Washington University School of Medicine) also loves to teach. "It really is very rewarding to see students stimulated in the same fashion that I was by the people who were so instrumental in my career," Aach states. "I think one of the most important missions a clinical scholar can be involved in is that of passing information on to a new generation of people who, hopefully, will perpetuate our knowledge and our approach to problems and diseases, and not necessarily the answers, but at least, the interest is finding the answers. I have been given the unique opportunity to do what I could as a physician, academician and clinician, to the best of my ability, without any limitations. I would like to see the same kind of environment supported to ensure that medical knowledge continues to advance at a rapid pace and that future generations receive the very best health care."

Lorna Williams is a St. Louis-based freelance writer.
Beckett Howorth, M.D. '25, wrote to say that he especially enjoyed an article in the last issue of Outlook, "Rare Books and Archives: Unearthing the Treasure." Howorth, a resident of Jackson (MS), has contributed many of his personal papers to the W.U. archives.

Howorth and his wife have provided for a chair in orthopedics at U. of Mississippi Medical Center. He writes that the hospital is producing a room in his honor, complete with memorabilia from his years of practice.

C. Barber Mueller, M.D. '42, received the Distinguished Service Award from the American College of Surgeons. Mueller is professor emeritus of surgery at McMaster University in Hamilton, Ontario.

Mueller completed internship and residency at Barnes Hospital. After a fellowship in biochemistry at Harvard, he returned to W.U. as a fellow in surgery. His work there included five years as faculty member in the Department of Surgery.

From 1956-67, he was professor of surgery and department chairman at Upstate Medical Center, SUNY (Syracuse). At McMaster, he served as professor of surgery and department chairman for five years.

Mueller is a Fellow of the Royal College of Surgeons (C), a member of the American Board of Surgery, the American Surgical Association, the Association of American Medical Colleges, and several Canadian professional organizations.

Virgil Loeb, Jr., M.D. '44, has received the First Annual Wendell G. Scott, M.D. Memorial Award from the American College of Surgeons. Currently, Loeb practices hematology/oncology in St. Louis and is president of the Missouri division of the ACS. He chairs the medical and scientific committee for the ACS's national board.

Walter A. German, M.D. '51, will be installed as president of the Missouri State Medical Association in April. The MSMA enrolls nearly 7,000 physicians in Missouri.

German is an ob/gyn from Springfield (MO). After earning an A.B. and M.D. from Washington U., he completed an internship at Jackson Memorial Hospital and residency at Grady Memorial Hospital. He has held office and served on committees with the MSMA and the Greene County Medical Society. German has served as president of the Missouri OB-GYN Society and the Springfield OB-GYN Society. Currently, he is president of the Springfield Clinic Corp.

Richard M. Krause, M.D. '52, assumed the position of Dean, Emory University School of Medicine, in July 1984. He was also named Robert W. Woodruff Professor of Medicine.

Krause came to Emory after nine years as director of the National Institute of Allergy and Infectious Disease at NIH. There, he reorganized research in microbiology and immunology and developed new programs in asthma and other allergic diseases, sexually transmitted diseases, and tropical medicine. Previously, he had been at Rockefeller University. From 1962 to 1966, he was on the faculty of W.U. School of Medicine, serving as professor of epidemiology and medicine.

Krause was a member of the house staff at Barnes Hospital. He was part of a research team that received the Lasker Award in 1954 for their work on the relationship between streptococcal sore throat and rheumatic fever.

Richard M. Krause, M.D.

While at Rockefeller University, his work in immunology laid the foundation for present-day work on the immunochemistry of streptococcal group-specific polysaccharides.

A chapter from his book, The Restless Tide: The Persistent Challenge of the Microbial World, was reprinted in the 1984 issue of Medicine at Emory. In it, he describes the effects of our "age of diminishing expectations" on the curiosity in the minds of those students of medicine currently being educated. In particular, he notes that there is a pressure to reduce our current investment in research, a vital part of any medical education.

Irving Kushner, M.D. '54, is editor of Understanding Arthritis, a new book written by the medical staff of the Arthritis Foundation. The book, published by Charles Scribner's Sons (New York), describes various treatments for several forms of arthritis. It also evaluates controversial treatments, such as DMSO, and includes information on preventive measures and diet.

Kushner is professor of medicine at Case Western Reserve University in Cleveland and director of rheumatology at Cleveland Metropolitan General / Highland View Hospital. He is also associate director of the hospital's Department of Medicine.

A long-time member of the American Rheumatism Association, he served as regional president. Member of several committees of the Arthritis Foundation, he chaired its review panel for medical and scientific publications.

S. Michael Freiman, M.D. '55, clinical associate professor of obstetrics and gynecology, recently went on a 13-day trip through China, accompanied by Professor Stanley Spector, director of Stix International House, Nanjing (St. Louis' sister city), Beijing, and Shanghai were part of the itinerary.

Freiman reports that China is
in a process of change, with the political, economic and medical care systems in a process of westernization. Acupuncture and traditional medical treatments are being replaced by the medical systems and technology of the West.

60s

Robert H. Waldman, M.D. '63, is professor and chairman of the Department of Medicine at West Virginia University. He writes in response to Morton Smith's editorial describing the limited usefulness of the MCAT and similar tests: "The MCAT... may have a negative impact on our successful students... We have set up an educational system which consists of a pathway interrupted (some might say assisted) by a series of hurdles. Some of these hurdles are small (courses with their final exams), and some are big (passage of board exams). This relatively short period of very intense, goal-oriented labor is followed fairly soon by a result, successful or not. So what happens at the end of [medical training], with its prolongation of adolescence and ingrained habits? If the trained and certified physician enters academic medicine, the habits are continued with the ritual of NIH grant application... [For] physicians who enter private practice, [the habit] may result in a problem practitioner left with no remaining medical goals... This results in the search for other types of immediate gratification — fancy cars, bigger houses... Is our testing system contributing to the level of greed exhibited by some physicians?"

Robert G. Scheibe, M.D. '64, has been elected president and chief of the medical staff at Missouri Baptist Hospital (St. Louis). A member of the hospital staff since 1973, he practices urology.

Jeannie Jones Kinzie, M.D. '65, has been named director of the division of radiation oncology in the Department of Radiology at the University of Colorado, effective July 1, 1985. The subject of an article in the Winter 1984 Outlook, Kinzie writes that she is pleased to be going back to her native home in the Rocky Mountains.

Phillip O. Periman, M.D. '65, is medical director of the Harrington Cancer Center in Amarillo (TX). A hematologist/oncologist, the Amarillo native recently wrote an editorial describing progress in cancer research. It was published in the Amarillo "News Globe."

70s

Christopher F. Blodi, M.D. '79, has been named assistant professor of ophthalmology at the Bascom Palmer Eye Institute at the University of Miami (FL). Blodi specializes in retina-vitreous surgery. Formerly, Blodi was in the Department of Ophthalmology at the University of Iowa.

C. Leon Partain, M.D./Ph.D. '75, has been promoted to Professor, Department of Radiology and Radiological Sciences, at Vanderbilt University.

80s

Steven A. Meador, M.D. '81, has been appointed instructor in the Department of Medicine, division of emergency medicine, at Hershey Medical Center (PA). Previously, Meador served on staff at the Hutzell Hospital in Detroit. In 1983, he was a medical team member with the Detroit Grand Prix II. He also served a summer externship with the USPHS and performed research in pediatrics oncology at NCI.

A native of Washington, D.C., Meador served his residency in emergency medicine at Wayne State University/Detroit Receiving Hospital.

Robert R. Goodin, FHS at Barnes Hospital (1964-66), is director of cardiology at Humana Hospital Audubon in Louisville (KY).

Thomas D. Miale, FHS, has been appointed to the Department of Pediatrics at Southern Illinois University (Springfield). Formerly, Miale was in the Department of Pediatrics at the University of Illinois College of Medicine (Chicago).

Carol E. Williams, FHS at Barnes Hospital (1957-60), is the first woman to be elected president of the St. Louis Metropolitan Medical Society. Her father, the late Daniel Williams, was once president with Allan M. Lansing, performing cardiovascular and thoracic surgery.

Barbie is board-certified in surgery and thoracic surgery. Formerly, he was chief of general and thoracic surgery at the U.S. Army Hospital at Fort Polk (LA). He received the A.B. from the University of Missouri (Columbia) and the M.D. from Tulane.

Donald K. Chung, FHS, a cardiologist and internist practicing in Long Beach (CA), recently made his first trip back to his homeland of North Korea since he left over 30 years ago. After serving for three years with the ROK Army, he attended premedical school in Seoul. He completed his medical training, internship and residency at Washington U.

Chung and his sisters were reunited on his recent visit, and he accepted an invitation to lecture in China. Chung's visit was an extremely rare privilege granted to any American, even one who is North Korean by birth.

Robert R. Goodin, FHS at Barnes Hospital (1964-66), is director of cardiology at Humana Hospital Audubon in Louisville (KY).

HEALTHPROS

Norma J. Long has been appointed the first dean of the School of Nursing at Memphis State University. Long was formerly professor of nursing and associate dean of undergraduate studies at the University of Mississippi School of Nursing.

A native of Arkansas, Long holds the bachelor's degree in nursing from the University of Arkansas and a master's degree in nursing from Washington U. She earned a doctorate in nursing science from Catholic U. Before joining U. Miss. in 1982, Long held several academic positions at the U. of Tennessee College of Nursing from 1967-81. Prior to leaving UT, she was associate dean and director of academic affairs at the College of Nursing. She also taught at the U. of Arkansas and Washington U.

South American Adventure

Dear Alumni:

Last May, you presented me with a gift certificate to "The Galapagos via Alumni Flights Abroad." Not only was I surprised, but I was also most pleased. (I shouldn't have been surprised, because I know you do wonderful things.) The trip (Nov. 28 - Dec. 9) was great in every way!

Alumni Flights Abroad, a rather new tour agency, took perfect care of my travel needs, in a generous and considerate way. Our guide, Miss Beatriz Diaz, was always extending her hand to me on the rough climbs.

The Galapagos Islands really can't be understood without experiencing them. Walking up the sides of each of 11 volcanoes, over large, sharp-edged hunks of lava, was extremely difficult but well worth the effort.

I was able to stroke a tortoise's neck and realize that he (if the tail was long) or she (if the tail was short) liked it. Finches looked like any of the island's 13 species, until a second look through binoculars showed the bill to better advantage and confirmed Darwin's superiority as a naturalist. The magnificent frigate bird was always beautiful in configuration and movement, and the outlandishly striking conduct of courting males showed the bright red color of their enormously puffed-out throats. The poor undersized penguins seemed to wish for a more southern clime, and the flightless cormorant waved his puny wings but was never able to get into the air. Marine iguanas had a fascinating ugliness, and I remembered to give a wide berth when passing them along the shore.

After bussing through the Andes, we spent the last three days in Quito (altitude 9,000 feet and over) and the surrounding countryside. Our headquarters was a well laid out, large hacienda from which we went to visit markets. A large animal market with cows, sheep, goats, pigs and chickens was much fun for Gladys and me because both of us have first-hand experience on a farm. A very large market displayed handmade sweaters, blankets, belts, etc., from sheep's wool. And a number of shops had paintings, wood sculptures and jewelry. Indians, all derived from ancient Incas, were everywhere although unobtrusive.

The entire journey was more fun and more interesting than I could have dreamed. And I do dream! I very much appreciate this unexpected and generous gift.

Many thanks and with love,
Mildred Trotter, Ph.D.
Professor Emerita and Lecturer
Department of Anatomy and Neurobiology

Ed. note: On a recent trip to Africa, Mildred Trotter suffered a stroke. This letter was written by her before she left.
The East Building, purchased several years ago by the university, has recently undergone complete renovation. It now houses an MRI (magnetic resonance imaging) facility containing a 20 kilogauss magnet, as well as a film library, computer installation and other components of the Department of Radiology. Other facilities in the East Building include the Program in Physical Therapy, the medical and dental bookstore, and several office suites.
"When Fear Strikes," page 12, describes a study performed at the School of Medicine on adults with a history of panic disorder. This is a PET scan of the brain of a sufferer from anxiety attacks, obtained after researchers infused a radioactive solution of lactate (known to precipitate panic attacks in susceptible persons). The image shows marked difference in blood flow between the right and left sides of the brain.