

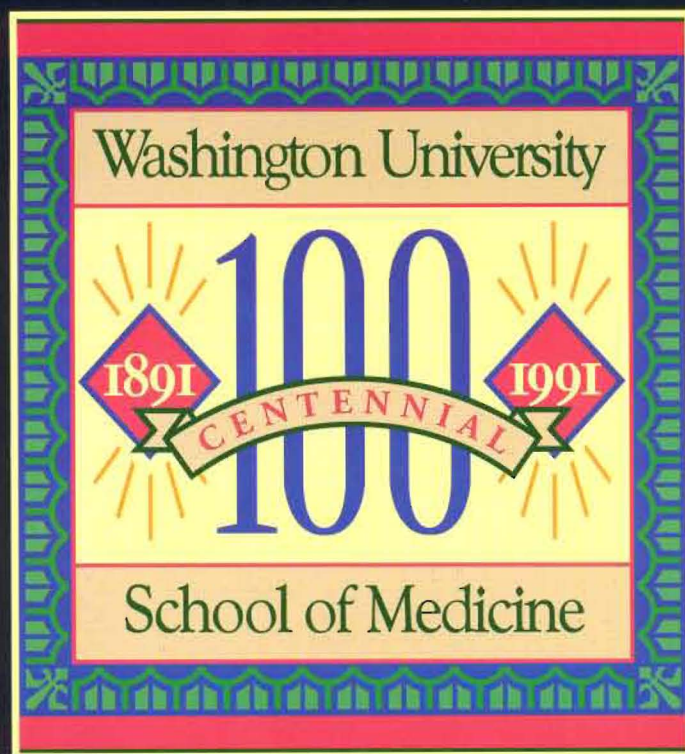
# OUTLOOK

A large, circular PET scanner assembly is shown, featuring numerous green circuit boards and a dense network of copper wires. The wires are bundled and connected to the boards, which are arranged in a circular pattern. The image is a close-up, showing the intricate details of the electronic components and the complex wiring.

More to gain  
from PET



**N**EXT YEAR, the School of Medicine celebrates its centennial. The School was formed in 1891 when the St. Louis Medical College, which had been founded in 1842, became the Medical Department of Washington University. In 1899, the Medical College, which had been in operation since 1840, joined the Department, thus uniting the two oldest medical schools west of the Mississippi River. Today, the Washington



University School of Medicine continues as one of the most outstanding medical schools in the world. A birthday celebration has been scheduled for October 9-12, 1991 that will include scientific programs and social events. Other special events are being planned to commemorate this milestone year in the history of the Washington University School of Medicine.

**JOIN IN THE CELEBRATION**



# OUTLOOK

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School of Medicine



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Outlook recalls the April 1915 dedication  
of the School of Medicine's first three buildings.

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Cardiologists use positron emission  
tomography to produce images of the heart.

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The Medical Genetics Division at Children's  
Hospital helps families that are affected by  
genetic disorders.

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### On the Cover:

An inside view of a PET (positron  
emission tomography) machine.  
PET was developed at Washington  
University by Michel M. Ter-  
Pogossian, Ph.D., and Cardiovas-  
cular Division scientists and physi-  
cians have been instrumental in the  
development of this technology.  
Barnes Hospital is the only hospital  
in the country with a PET scanner in  
the Cardiac Care Unit, which allows  
evaluation of acutely ill patients.  
See story on page 14.

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## Diabetic off insulin after islet transplant

A 36-year-old female patient who received a transplant of insulin-producing cells isolated from cadaver pancreases was successfully off insulin injections for more than two weeks, Washington University researchers have reported in a recent issue of the journal, *Diabetes*.

The patient is one of several who received pancreatic islet cell transplants through pilot clinical trials at the School of Medicine's Clinical Research Center and Barnes Hospital. The transplanted cells are removed from the pancreas's "islets," pockets of hormone-producing tissue that release insulin. Within 10 days of receiving the new islets, the patient no longer required daily injections of insulin. The patient remained insulin-independent until the 25th day after transplantation, when evidence of tissue rejection appeared and the patient began to require gradually increasing amounts of supplemental insulin. At this point there is no evidence of continuing graft function.

This case marks the first time that transplanting purified, isolated cells has eradicated the need for insulin injections in a patient with juvenile-onset diabetes. Researchers had until now accomplished only a partial reduction in patients' needs for insulin.

"We are immensely pleased that the grafted tissue was able to satisfy all of the patient's insulin requirements before it was rejected," said David Scharp, M.D., the surgeon who conducted the transplant. "Our first trials, in 1985, were



**Islet Lab.**

designed to determine that islet transplants were safe. In this study, our primary goal was to determine if we could isolate, purify and transplant enough islets to bring a patient completely off of insulin." Paul Lacy, M.D., Ph.D., the Washington University pathologist who devised many of the techniques used to isolate and purify human islets, said this patient's case "shows that islet transplantation is a feasible approach to controlling insulin-dependent diabetes and clearly establishes the need to move on to larger clinical trials. Rejection, which prevents our ability to keep the patient off of insulin long-term, is a totally separate problem, and our previous research gives us many good ideas about how to combat rejection in future trials."

Scharp added: "While these results are an important step

forward, many more years of research may be needed before islet transplantation can become a routine treatment for diabetics."

The patient reported in *Diabetes* received approximately 800,000 islets isolated from two cadaver pancreases. The islets were 95 percent pure, according to the researchers, and were tested to confirm their ability to produce insulin. The patient was under local anesthesia when the islets were injected into the liver. The insulin production of the transplant was determined through precise measurements of C-peptide, a precursory fragment of the insulin molecule that is released from islet cells along with intact insulin.

In the transplant procedure, insulin-producing cells are harvested and purified from one or more cadaver pan-

creases, then injected into a patient's liver. Once established, the cells act as a natural source of insulin and reduce or obviate the need for daily injections. These clinical trials are limited to diabetics with no insulin production who have either a previous or simultaneous kidney transplant and are immune-suppressed with cyclosporin and other medications. The researchers were hopeful that the immune suppression used to maintain the kidney transplant would also protect the islets from rejection.

The Washington University Human Islet Transplantation Center has agreements with three universities for expanded clinical trials in diabetic patients who are to receive a kidney transplant: University of Western Ontario at London, Ontario; University of Florida at Gainesville; and University of Pennsylvania in Philadelphia. Researchers collaborating with Lacy and Scharp will send a pancreas to St. Louis for islet isolation. The islets will quickly be returned and transplanted, along with the same donor's kidney, into a patient with juvenile-onset diabetes. The combined kidney/islet transplants will be conducted according to protocols approved by both Washington University and the collaborating institution. ■

Note: Just before this issue of Outlook went to press Lacy and Scharp presented new data on the status of these pilot studies and reported that they now have a male transplant recipient who remains insulin-independent seven weeks post-transplant. The status of this patient and all others in the clinical trials was presented at the Annual Meeting of The American Society of Transplant Surgeons and will be submitted for publication in the journal, *Transplantation*.



## Vice Chancellor Peck reorganizes administration

**W**illiam A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine, has made several new administrative appointments.

Patricia L. Cole, M.D., has been named associate dean for student affairs. Cole has been on the faculty for four years and is an assistant professor of medicine. She is the director of invasive cardiology training at Jewish Hospital, where her clinical emphasis is cardiac catheterization and balloon angioplasty. In her new role she will be responsible for dealing with students' academic affairs, assisting them with financial aid, reviewing clerkship reports and supervising operation of Olin Residence Hall.

W. Edwin Dodson, M.D., has accepted the position of associate dean for admissions and will be responsible for planning and managing the admissions programs at the School of Medicine. Dodson has been with the school since 1971 and for the last four years has been a professor of pediatrics and neurology. He is involved in the research of severe epilepsy and its treatment and also has an active interest in the prevention of child abuse.

The appointments of Cole and Dodson became effective on July 1, when John C. Herweg, M.D., retired as associate dean of the School of Medicine. Sharing Herweg's responsibilities enables Cole and Dodson to continue their research and clinical activities.

Carl D. Rhodes, Jr., Ph.D.,

has been named associate dean for graduate studies at the School of Medicine as well as associate dean in the Graduate School of Arts and Sciences. Rhodes' primary responsibility will be to serve as chief academic administrator for the six interdepartmental Ph.D. programs in the Division of Biology and Biomedical Sciences. Rhodes, who was at Washington University from 1983 to 1988 and at the University of Texas Southwestern Medical Center from 1988 to July 1990, also received two faculty appointments: research professor of biochemistry and molecular biophysics, and professor of biology.

Thomas R. Sonderegger has been promoted to assistant vice chancellor and assistant dean. Sonderegger has been on the medical school staff 12 years, the last five as director of strategic planning, responsible for enhancing financial planning systems. He has been responsible for developing strategies for the allocation of resources, creating financial forecast models and participating in long-range planning efforts. In his new post he will continue directing that area and will also develop systems to study and plan for the expansion of clinical and research facilities, to facilitate departmental financial planning and to coordinate strategic planning efforts between the medical school's clinical departments and Barnes Hospital.

Valorie J. Hambley has been named assistant dean for

administration. Her primary responsibilities in this new post are research administration and human resource management. For the last seven years, Hambley has served as administrator for the Department of Pharmacology, responsible for handling grants, personnel, payroll and finances. She also acted as a liaison between researchers, university administration and outside funding agencies and for a brief period worked as interim co-business manager for the Office of Animal Laboratory Care.

Glenda K. Wiman, formerly the executive director of medical public affairs, has been appointed assistant dean for special programs. In this newly created position, Wiman will have a broad range of activities including coordinating the National Council of the School of Medicine, developing continuing education programs, assisting in the development of department head, faculty and student recruitment programs and initiating new corporate and community relations efforts. Wiman has been in the Office of Medical Public Affairs for more than 15 years, serving as director since 1981 and executive director since 1987.

Donald Clayton has been appointed the new executive director of medical public affairs. Clayton has worked at the School of Medicine for eight years, most recently as director of medical public relations. He will supervise the media relations, publications and photographic services. ■

## Hortin receives Culpeper Scholarship

**G**len Hortin, M.D., Ph.D., assistant professor in pediatrics and pathology at Washington University School of Medicine in St. Louis, recently received the Charles E. Culpeper Foundation Scholarship in Medical Science for 1990.

With this award, Hortin will receive \$100,000 a year



*Glen Hortin, M.D., Ph.D.*

for three years to fund his research into the interactions of a family of immune-system molecules called complement. Hortin's interest is in the basic operation of the complement "cascade," a series of consecutive reactions in which complement molecules interact with one another like dominoes, one's activity triggering that of the next.

The cascade is activated by the binding of antibodies to invading bacteria or other foreign particles. As a result, bacteria are killed and foreign



particles marked for uptake into white blood cells.

In some autoimmune diseases, such as systemic lupus erythematosus, the complement system attacks the body's own cells as well as bacteria. In this illness, characterized by fever, fatigue and skin lesions, complement activation contributes to kidney failure and damage to other vital organs. Hortin seeks to find ways to shut down the complement system when it is damaging normal tissues.

The scholarship program was established in 1987 as an extension of the Culpeper Foundation's ongoing commitment to medical science, which has totalled approximately \$20 million since 1970. The foundation is a private, non-profit charitable organization established under the will of the late Charles E. Culpeper, one of the early pioneers in the bottling and marketing of Coca-Cola. In recent years, the 50-year-old foundation has awarded more than \$6 million annually to activities in health, science, technology, education, the arts and administration of justice.

Hortin was one of three researchers selected nationwide from among 50 applicants nominated by their respective institutions. The objective of the program is to support high-achieving young physicians who are committed to careers in academic medicine. ■



**Robert P. Perrillo, M.D., principal investigator of the multicenter hepatitis B study, and research nurse Carol Bodicky successfully used interferon to treat patients with chronic hepatitis B.**

## Interferon therapy cures hepatitis B in 11 patients

**A**n intensive course of interferon therapy induced remission of chronic hepatitis B in 38 of 126 treated patients and completely cured 11 of those who achieved remission, according to the results of a multicenter, 169-patient study coordinated by Robert P. Perrillo, M.D., an associate professor of medicine at Washington University. The study was published in August in the *New England Journal of Medicine*.

Chronic hepatitis B is a serious, debilitating, infectious liver disorder that predisposes to cirrhosis and can be fatal. There has previously been no cure for the disease. An estimated 1 million Americans are chronically infected with the hepatitis B virus, and the risk of primary liver cancer is at least 100-fold greater in those individuals. The multicenter study included trials at 12 research centers and is the first large, controlled study of its kind.

"We can cure people who might otherwise have a life-long infection with serious consequences if we get to them early enough," says Perrillo, who is also director of gastroenterology at the Veterans Administration Medical Center in St. Louis and served as the study's principal investigator.

Most cures occurred in patients who had hepatitis B for two years or less. Response was determined by measuring the amount of replicating virus in a patient's blood. "Cure" was defined as the complete disappearance of virus. Patients in "remission" are those in whom the virus became inactive and symptoms disappeared. Tests of viral replication were made throughout the treatment period and at one, three and six months after treatment.

"If you've had your hepatitis less than two years, your chances of getting rid of the disease are much better," Perrillo says. "We believe this

indicates that early in the infection the virus does not integrate its genetic material into the host cell genetic material. But if enough time goes by, it does, at which point total eradication of the virus may be impossible."

The study reports fatigue as the most common side effect associated with interferon therapy. Other flu-like symptoms that occurred included fever, headache and myalgia, but these improved as therapy continued.

At this time, interferon is not federally licensed to be used in the treatment of hepatitis. Perrillo says the encouraging study results may hasten federal approval.

"We have made a significant step, but long-term follow-up will be necessary to determine the frequency of disease relapse and long-range benefits," Perrillo says. "I think we can feel confident in telling patients that our rate of successful treatment with interferon therapy is about 50 percent overall." ■



## Molecular “billboard” for spinal cord neurons

Scientists at the School of Medicine have reported the first evidence that as the brain develops, it employs a sort of molecular “billboard” to coax axons — which transmit impulses from nerve cell to nerve cell — to grow into a part of the brain that controls motor behavior.

The research concludes that a part of the brainstem called the basilar pons releases a molecule that beckons to nearby axons, inducing them to bud and extend branches. This chemical signal influences axons traveling along a path from the neocortex to the spinal cord and in this way initiates the formation of a major connection that is essential for controlling movement.

The findings, published in *Science*, may have long-range implications for the treatment of spinal cord injuries that cause breaks in connections from the motor cortex to the spinal cord.

“This molecule clearly influences the growth of cortico-spinal axons,” explains Dennis D.M. O’Leary, Ph.D., the neuroscientist who heads the research team. “By studying the cellular events in this process, we can better understand what is involved in axon guidance and branching. This is crucial to attaining regrowth and forming proper connections after spinal injury in adults.”

O’Leary plans to collaborate with a biotechnology firm to isolate the molecule. He cautions that research on this novel activity is in the very early stages, but adds, “If we can isolate and characterize

this molecule, it might be useful to help induce cortico-spinal axons to re-establish their connections after spinal injury.”

The mechanism that O’Leary and his colleagues describe, called chemotropism, was first suggested by Nobel Prize-winning Spanish neuroanatomist Ramon y Cajal near the turn of the century, but discarded for want of evidence. The theory has only recently gained experimental support.

“Our results provide the first evidence that in the developing brain, axon targets can influence the direction of axon growth and the formation of branches,” says O’Leary.

For this project, part of a series of studies examining how the neocortex develops and acquires specific features, the Washington University scientists studied axons from layer 5 of the six-layered neocortex. Initially, layer 5 axons grow out of the cortex and into the spinal cord, bypassing their targets in the brainstem. Only later do they form branches at the appropriate locations along their length. The branches then grow and contact their targets, including the basilar pons, which acts as a “switchboard” between the neocortex and the cerebellum.

What cues prompt these branches to form and choose their targets? To answer that question, O’Leary and neurosurgery resident Christopher D. Heffner, M.D., used a three-dimensional collagen matrix, into which they embedded pieces of developing cortex, basilar pons and other neural structures. The matrix

enabled them to look for activity generated by the basilar pons. They found that in this setting the basilar pons releases a diffusible molecule that induces the formation and directional growth of branches from layer 5 axons. Based on this evidence, they suggest that in the developing brain, the molecule spreads into the cortico-spinal axon track; there, it functions as a sort of “billboard,” inducing axons to form branches and providing cues to direct their growth into the basilar pons.

Until now, the prevailing opinion has been that the primary growth cone — or leading tip — of the axon is responsible for target selection. But in a previous article published in the journal *Neuron*, O’Leary and colleague Toshio Terashima, M.D., reported a different role for the primary growth cones of layer 5 axons.

They found that growth cones guide the primary axons

of layer 5 neurons as they travel a path past the pons and into the spinal cord. However, the growth cones have no role in selecting the basilar pons as a target; rather, this is accomplished by the later branching of the cortico-spinal primary axons. That process they now attribute to the molecule released by the maturing basilar pons.

“These findings will force us to re-evaluate the role of the growth cone in axon targeting,” says O’Leary. “Our evidence, together with that recently obtained in other labs, establishes the long-neglected chemotropism as a viable means for setting up neural connections.”

Eventually, the Washington University scientists hope to isolate the diffusible molecule they have identified and then clone its gene. “Applications to medicine are still light years away,” O’Leary says, “but the potential is very exciting.” ■

## MERIT status for Kornfelds

Stuart A. Kornfeld, M.D., and Rosalind Kornfeld, Ph.D., professors of medicine and biochemistry, have received MERIT status from the National Institutes of Health (NIH) for their latest grant. The five-year grant from the National Cancer Institute totals \$1,715,912. The funding will enable the Kornfelds to continue research on the biochemistry of glycoproteins.

Researchers cannot apply for MERIT status, but are chosen in recognition of their

consistent commitment to excellence based on previous research. Once received, a five-year grant with MERIT status may be extended an additional three to five years, based on an expedited review of work accomplished during the initial period.

“Work in the Kornfeld laboratory has led to a much greater understanding of certain rare disorders called lysosomal storage diseases,” said William H. Danforth, M.D., chancellor of Washington University. “This research ultimately could lead to the development of new therapies to treat these diseases, which can be crippling and even



lethal. We are pleased that NIH has recognized their outstanding efforts with this honor."

The Kornfelds have helped to explain how glycoproteins, molecules with sugar and protein components, are synthesized by cells. In particular, they have elucidated the complex machinery used by cells to form the carbohydrate units of glycoproteins. These carbohydrates are of interest because they serve as recognition molecules that target proteins to particular locations in the cell, such as the lysosome, the cell's "garbage disposal."

The Kornfelds have shown that a deficiency of one of the carbohydrate biosynthesis enzymes leads to the breakdown in the targeting of specific proteins (lysosomal enzymes) to lysosomes. This, in turn, causes accumulation of undigested "garbage" in the cell.

The information on protein targeting and the role of the lysosome may be used in the future to develop new therapies for detecting and treating a family of metabolic disorders that are rare but very serious. ■

thinks that, concurrently, unused fatty acids accumulate along with carnitine, a naturally occurring amino acid that binds to and carries fatty acids into and out of the mitochondria — the cell structures responsible for generating energy. Those accumulations have a poisonous effect on the infant's system. Describing the buildup, Strauss says, "The elements are highly toxic; if you inject carnitine bound to a fatty acid into a heart muscle, it stops immediately."

In less severe cases, infants sometimes arrive at emergency rooms with symptoms much like those of Reye's syndrome: low blood sugar, liver failure and vomiting. A quick, intravenous dose of sugar, Strauss says, is the medicine they need. Terrifying for parents, such a non-lethal event might actually be a blessing in disguise because it identifies a youngster at risk. Further trouble can be avoided by guaranteeing regular food intake or, at worst, intravenous sugar when the child can't eat, Strauss says.

"This deficiency occurs in about one of every 5,000 children, so it's not uncommon," says Daniel P. Kelly, M.D., an instructor of medicine at Washington University and one of Strauss' collaborators. When a child is identified as deficient, family members are screened, but Kelly and Strauss would prefer a screening test that is more readily available. That will require uncovering the precise genetic mechanism by which the faulty enzyme occurs.

However, that mechanism is complicated and elusive. The gene that codes for the enzyme does not appear to be the culprit. "In many inherited enzyme deficiencies," says

Strauss, "a mutation on the gene results in an inefficient protein. Here, the problem is something else. The gene in deficient patients and in normal controls appears to be identical."

So far, the investigators have traced the trouble to the process by which precursor RNA is "spliced" to become messenger RNA. The procedure, simply put, goes like this: The gene, made up of informational islands (exons) within the DNA molecule is copied first into precursor RNA. Most genetic flaws occur in the gene and are passed along into the first copy. The precursor RNA is then "spliced." In this step, only the informational bits are preserved; non-instructive elements (introns) are eliminated. The result is a compact recipe for a protein, called messenger RNA. Finally, the RNA leaves the cell nucleus with the instructions for making the protein. In this case, the protein is the enzyme known as MCAD.

By working backward from MCAD to its garbled messenger RNA and then to its normal precursor RNA, the researchers have found the locus of the problem. The deficiencies that Strauss reports occur as a result of one or a combination of 15 different problems in splicing. The instructions get confused, and the product is "a mess," Strauss says.

For the moment, MCAD deficiency stands as the lone example of what may be a new class of genetic disorders — those attributable not to the genes themselves but to the splicing process that is still poorly understood, though undoubtedly controlled by other genes. ■

## Tracking down SIDS

**T**he first biochemical evidence of one cause for sudden infant death syndrome (SIDS) is in, and it implicates a flaw in how genetic instructions are decoded. Researchers believe the misinterpretation results in a faulty enzyme that can't do its job of converting fatty acids into energy. Raw materials subsequently build up to toxic levels and, too often, an affected infant succumbs to a combination of fuel starvation and self-poisoning.

Experts in the field agree that SIDS deaths occur from a variety of causes, most of which remain mysterious. The flaw that results in the enzyme deficiency may be at the root of only 5 to 10 percent of the total.

But in those cases, the problem is with "one of the three enzymes that catalyze

the first step in turning fatty acids into fuel for energy," explains Arnold W. Strauss, M.D. A professor of pediatrics and biochemistry, Strauss proposes a scenario for this type of SIDS: Usually babies producing a faulty enzyme do fine. They get their energy from glucose and glycogen, and the deficiency remains silent. But, if for some reason — illness, simple colic or pure accident — an affected infant doesn't eat for about 15 hours, trouble occurs.

"That's the threshold," Strauss says. He explains that sugars provide a human's fuel for only four or five hours, after which the body shifts smoothly to fatty acids as its main source of energy. But if the changeover is impaired by a faulty enzyme, energy gradually becomes unavailable. The first organs to fail are the biggest energy users: the heart, the brain and the liver.

The lack of fuel alone probably won't kill as rapidly as SIDS strikes, Strauss says. He

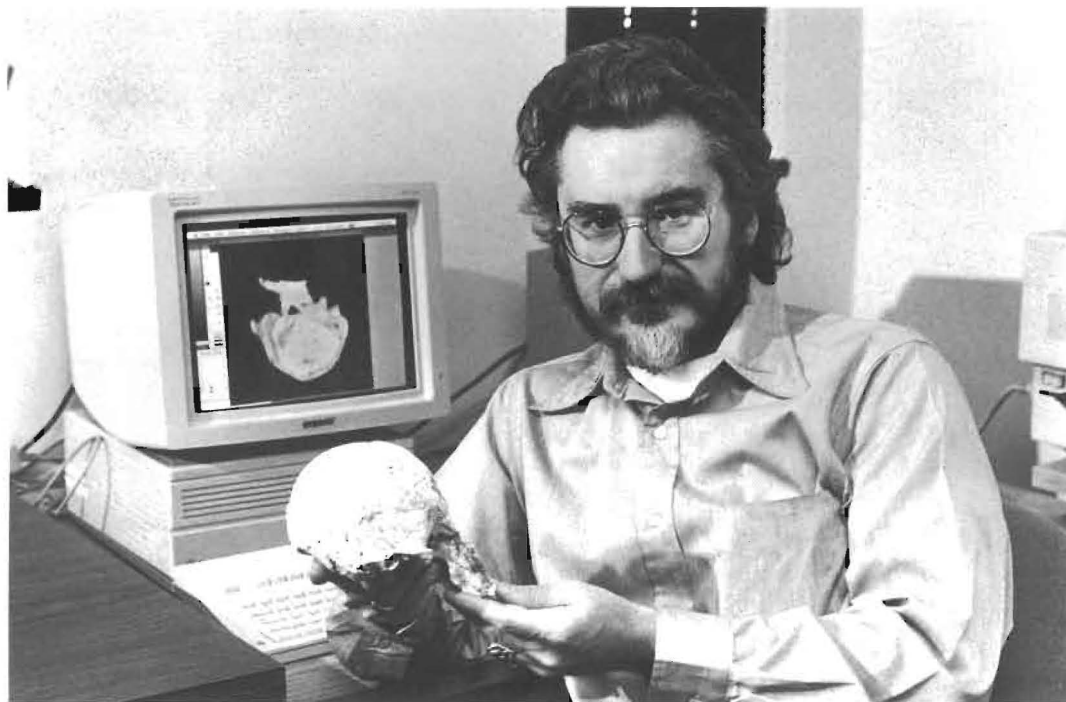


## Reading old bones

A 2-million-year-old, fist-sized lump of rock is helping scientists pry open one of the bottlenecks that has restricted a clear interpretation of human origins. The lump — really a stone-filled partial skull from a critically important era of deep prehistory — becomes only the sixth example of a pivotal ancestor in human evolution.

Applying advanced radiologic techniques, Glenn C. Conroy, Ph.D., and his colleagues have made available for study the previously uninterpretable skull that belonged to an animal of the species *Australopithecus africanus*, the earliest known hominid from southern Africa. For only the second time, a specially tuned computed tomography (CT) scanner has been used to see through the rock that fills a fossil skull, revealing the interior for study.

Though paleoanthropology is a field charged with controversy, many of its scientists believe that *Australopithecus africanus* may be in a direct ancestral line to modern humans. Small and newly bipedal, *A. africanus* moved from the forest to the hot savannas of Africa not too long (in evolutionary terms) before the explosion in brain size that has since characterized our species. It is therefore a creature of particular interest. But only six skulls identified as belonging to the species have been unearthed, and some of them have been less than ideally informative.



Glenn C. Conroy, Ph.D., used the CT scanner to coax information from hominid fossil.

Least helpful among the six has been the small, partial skull known only by its museum identification number: MLD 37/38. However, in a paper published in *Science*, Conroy and his colleagues, Michael W. Vannier, M.D., and Phillip V. Tobias, report on information they have coaxed that ancient skull to divulge.

Because MLD 37/38 is only about half of a complete skull, the anterior portion having eroded over the eons, accurate measurement of the cranial capacity has been impossible. In evolutionary studies, cranial capacity is often accepted as a close approximation of brain size, says Conroy, a professor of anthropology and anatomy. And for paleoanthropologists, precise measurement of a specimen's cranial capacity is important: it places a skull on the scale between apes and humans and relates brain size to other information about lifestyle and neurological organization — valuable data for theorizing about evolution-

ary trends and timetables.

Estimates of the capacity of MLD 37/38 by experts using external skull measurements have varied by about 10 percent, from 435 to 482 cubic centimeters. Such estimates are troublesome, Conroy says, because the fossil in question "has neither a modern human nor modern pongid (ape)-shaped skull," and those are the two large models on which such estimates are based. Because the skull is completely filled in with solid limestone, even measuring the thickness of the skull's bone has been impossible.

Using computer programs written for the task, Conroy and Vannier, a professor of radiology, achieved a precise value for the skull's capacity, putting to rest the controversy. Vannier adjusted the scanner to "see" through the rock that fills the cavity, enabling the investigators to make two-millimeter-thick image slices of the intact portion of the skull. The endocranial volumes were then computed.

The researchers also devel-

oped a new technique to reconstruct the missing parts of the skull, first computer-generating a slice that formed a symmetrical fit with the previous slice, then another on top of that one and so on. The generated slices were opacified on the computer screen and added to the stack. Half of the complete image's 46 slices were created in that way.

By adding the volume of the preserved portion to the volume of the reconstructed portion, they determined a total capacity for the skull. The result was a reliable figure of 425 cubic centimeters, at the low end of all previous estimates and, Conroy says, "the lowest endocranial capacity for any adult specimen of *A. africanus* to date."

As a result of the MLD 37/38 data, the mean cranial capacity for all known *A. africanus* examples drops to 440.3 centimeters, about one-third of a modern human's and roughly half that of our more recent ancestor, *Homo erectus*. ■



APRIL 28, 29, AND 30, 1915.

# THREE DAYS TO REMEMBER

BY M. KENTON KING, M.D.





*Barnes Hospital and the Washington University School of Medicine shortly after the 1915 dedication.*

**I**t happened 75 years ago. There was a huge medical celebration here at Euclid and Kingshighway in St. Louis. No event since has approached it in scope. The completion of the three original buildings of the School of Medicine called for a magnificent dedication. The new Barnes Hospital had been dedicated a few months before.

The whole nation was to hear about the new medical facility to be launched in the West. The three new buildings, of strikingly similar architecture, now referred to as South, North, and West buildings, would house the laboratories of the new school. (The West Building had been known as the Clinic Building during its first 45 years, because outpatients were seen there.)

Robert Somers Brookings had realized his dream. This truly remarkable man had worked steadily for six years to accomplish the tremendous facility now to be dedicated. As president of the Corporation of Washington University, Brookings had devoted most of his efforts, from 1909 to 1915, toward building a first-rate medical



school. The cause gripped his attention as not even the reorganization of Washington University had done before.

Brookings had come to St. Louis at the age of 17, and had been given a job by Samuel Cupples, a manufacturer's agent for all types of woodenware, from clothespins to wooden bowls and spoons. Young Robert had later become a member of the firm at age 21. He subsequently amassed a sizable fortune; but, in middle life, turned his abundant energy toward the university, first establishing the Lindell and Skinker campus, and then building an excellent medical school. Brookings himself had not graduated from high school.

Writing about Brookings and the new medical school, Hagedorn\* noted: "It was so completely alien to his past experience that he had no half knowledge to confuse him. He knew nothing of medical education, and he knew that he knew nothing, which was the beginning of wisdom. He visited Johns Hopkins and the newly completed Harvard Medical School, observing, conferring, asking unexpected, challenging questions, listening as he never had listened in his life. He went abroad and spent a year studying medical education in Great Britain and on the Continent... It did not seem to occur to him that the selection of a medical faculty might be regarded as outside his province. He had made the Medical School so completely his life, that he himself was unconscious that there were bounds to his authority."

Brookings had recruited the young men in 1910-11 who formed the nucleus of the original faculty: George Dock, M.D., in Internal Medicine, Philip Shaffer, Ph.D., (age 29) in Biochemistry, Eugene Opie, M.D., in Pathology, and Joseph Erlanger, M.D., in Physiology. It was Erlanger who had stipulated that the new faculty should be allowed to select their own dean. This was the beginning of the Executive Faculty system of governance for the school. Dock was selected to be the first dean, serving for two years. He was followed by Opie, who was dean at the time of the ceremony.

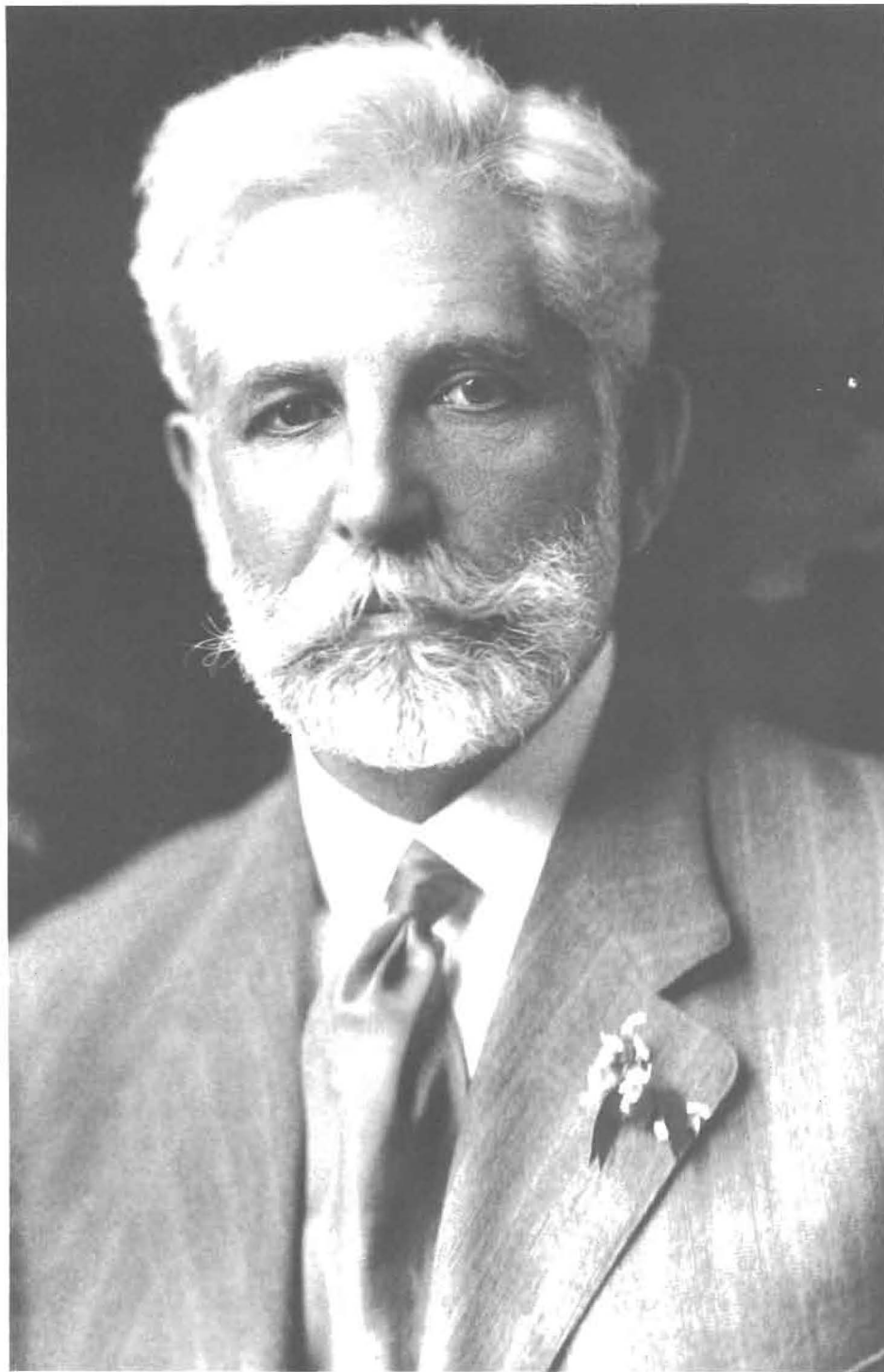
The dedication of the new building took place in April 1915. World War I was raging in Europe, but the United States would not enter for another two years. Women were not yet allowed to vote. Radio had not been invented. There were a few automobiles in the streets, but the horse and buggy was still dominant. Trolley cars

were the best means of transportation in the city. They were abundant.

From about 1830 to 1870, St. Louis had grown very rapidly. For a brief time, between 1870 and 1875, St. Louis laid claim to being the third largest city in the country. The census at the time, however, was disputed. The railroad became the primary means of cross country transportation between 1870 and 1915; and in April 1915,

St. Louis was a great rail center. Union Station was then nearly 20 years old.

The gala ceremonies began at 10 a.m. on Thursday, April 29. A procession formed in front of Barnes Hospital. The administrative officers of the university led the parade, as they do nowadays at commencement. The distinguished delegates from other universities



*Robert S. Brookings*

\* Hagedorn, Herman, *Brookings: a biography*, Macmillan 1936.



were next in line. These were followed by the guests and finally by the faculty of the medical school. At 10:30 a.m., exercises took place in the Assembly Hall in the North Building (today called the Carl V. Moore Auditorium).

The presiding officer was Acting Chancellor Frederic Aldin Hall. He introduced the Right Reverend Daniel Sylvester Tuttle, Bishop of the Diocese of Missouri, who offered a prayer. Chancellor Hall then introduced Robert Somers Brookings, president of the corporation.

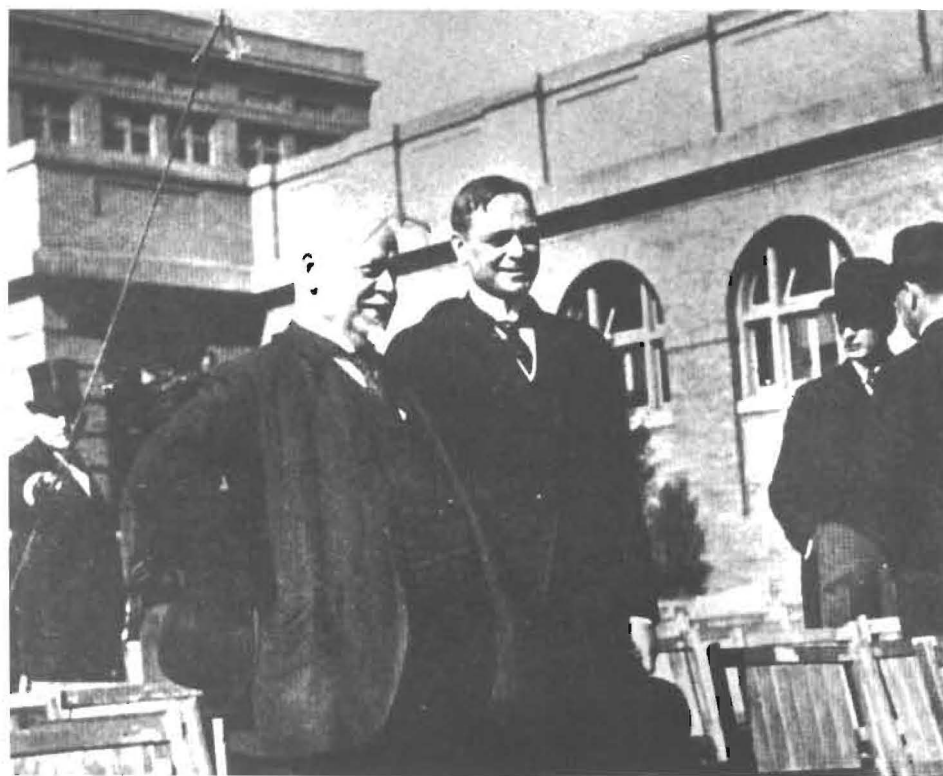
Brookings concluded his brief address as follows: "We hope that our efforts will contribute, in some measure, to raising the standard of medical education in the West, and that we will add, through research activities, our fair quota to the sum of the world's knowledge of medicine." In view of what has happened since, it was to be an understatement.

Johns Hopkins, and Simon Flexner of the Rockefeller Institute. A total of 33 other distinguished delegates were also presented.

Subsequently, an "Address for the Faculty by the Dean of the Medical School" was given by Opie (who was still working many years later at the Rockefeller University at the age of 95). Opie gave an address of some length. It is remarkable that he was the only speaker in the three-day period to mention World War I. He commented: "Whatever view is taken of the significance of the struggle which has possession of Europe few can deny that it brings into bold relief truths that are often forgotten. Science has no nationality, but national strength today is dependent upon the recognition of the value of science and its application to the routine of living."

Fifty-five years later, in 1970, Opie\*, looking back and writing at the Rockefeller University in New York, stated: "In an ad-

tablishment of a medical school of the highest type." Later he wrote some words which are priceless in giving us a clear firsthand picture of Robert Brookings: "The aims of Mr. Brookings, president of the corporation, were essentially identical with those of the medical group... He was anxious to obtain advice when medical problems were under consideration but was persuasive and preferred to talk rather than to listen. His usual procedure was to state the matter in his own terms and then talk about it, unless prevented, until he was about to leave; nevertheless, he would listen if urged and would change an opinion when he received good evidence to contradict it. He had no compelling urge to vindicate an opinion that he had once expressed. Without the enthusiasm of Mr. Brookings the reorganization of the school would not have been undertaken and financed."



*William H. Welch, M.D. (left) and George E. Vincent*

Following Brookings, Theodore Carl Link, the architect, presented the buildings. The keys were accepted by the chancellor. Walter Eugene Garrey, associate professor of physiology, then presented the delegates from other institutions of learning to Brookings and Hall. Among the presentees were President Abbott Lawrence Lowell of Harvard, Professor Rudolph Matas of Tulane, Professor Theodore Janeway of

dress at the dedication of the new buildings of the medical school, I described what seemed to me the spirit of the young men who had committed themselves to the es-

At the remarkable ceremonies of 1915, the speaker who followed Opie was William Henry Welch, M.D., of Johns Hopkins University. Judging from his status at the time, and perhaps from the length of his address, he was evidently the main speaker. His presence elevated the dedication of the new buildings to an event of national significance.

In the history of American medicine, no other person before or since has ever reached the pinnacle of public recognition as that achieved by Welch. If ever there was a man born at the right time, educated in all the right places, and elevated to prominence in a time of great need, it was William Henry Welch. Born in 1850, he graduated from medical school in this country and had studied physiology with Carl Ludwig in Leipzig in 1876. He learned pathology with Julius Cohnheim in Breslau in 1877, and took Robert Koch's course in bacteriology in 1885. Welch later discovered the bacillus which bears his name. He became professor of pathology and the first dean at the Johns Hopkins University School of Medicine.

Simon Flexner\* expresses the phenomenon of Welch in enviable prose: "At 35 Welch had found his place in the world... for many years a genie confined in a bottle, he rose up, once the cork was pulled, into his true dimensions, and for almost 50 years

\* Opie, E.L., *Adoption of Standards of the Best Medical Schools of Western Europe by those of the United States, Perspectives in Biology and Medicine*, Spring 1970.

\* Flexner, S., and Flexner, J.T., *William Henry Welch and the Heroic Age of American Medicine*, Dover 1966.



# Washington University



Henry Schwarz M.D.



Fred T. Murphy M.D.



Eugene L. OP



Robert J. Terry M.D.



Dennis E. Jackson Ph.D.

he was to tower over American medicine, determining, creating, helping change a backward profession into a leading profession of his time." He led American medicine away from the proprietary schools of the nineteenth century, and into the scientific era of the twentieth.

Welch was a lifelong bachelor, of ample girth, with a familiar mustache and goatee affectionately referred to as "Popsy". He was a father figure to two generations of young American scientists. Furthermore, he was always available to help launch new institutions, always ready to boost new programs in medical education and science. In 1930, on Welch's 80th birthday, President Hoover delivered a special broadcast on major radio networks: "Dr. Welch is our greatest statesman in the field of public health," he began. This tribute was broadcast across the ocean on short wave and retransmitted from London throughout the British Isles and on the Continent. Simultaneous ceremonies took place in London, Paris, Geneva and Tokyo. In this truly remarkable fashion, "Popsy's" 80th birthday was celebrated.

In St. Louis, in 1915, Welch began his address: "One of the most significant events in the recent history of medical education in America, significant especially for the South and West of this country, has been the reorganization of the Washington University medical school in accordance with the most advanced standards of modern

medical teaching and research." He continued a bit later: "I desire likewise to commend the high wisdom of the trustees of Barnes Hospital and of the St. Louis Children's Hospital, who, by entering into affiliation with the university and by placing the professional service in the hands of the medical faculty, have made these institutions freely available for teaching and the advancement of medical knowledge, thereby rendering them of far greater service than otherwise both to patients and to the community." Welch concluded his address by saying that the City of St. Louis must feel a justifiable pride in the new medical school.

After lunch on April 29, the weather having warmed up a bit, the addresses were continued on the lawn of the medical school between the North and South buildings (where the new library now stands). The speaker was President Abbott Lawrence Lowell of Harvard. Chancellor Hall introduced him with a deft historical touch: "Upon the formal inauguration of Washington University, April 22, 1857, Harvard College was called upon to furnish the orator of the

day in the person of Edward Everett. This afternoon, 58 years later... Harvard again contributes the first speaker, President Abbott Lawrence Lowell." President Lowell presented a dissertation on medicine as a public service.

One of the speakers later that afternoon, President George Edgar Vincent of the University of Minnesota, indicating his intention to speak briefly, acknowledged the thunderous noise of the street-cars on Euclid Avenue. He said: "The patient, self-controlled congregations in colonial New England were wont to watch with hope the spending hour-glass by the preacher's side. We have today, in these passing trolley cars, a modern equivalent of the old device. I understand that the periodicity of these rattling shuttles is about three minutes. Let me reassure you at the outset: I shall detain you only two or three cars." At 4 p.m. there was a garden party on the grounds of the medical school, and the guests were guided through the laboratories, and the Barnes Hospital, and St. Louis Children's Hospital.

On the morning of April 30, 1915, addresses of welcome were given in the Assembly Hall to the alumni of the medical school. Professor Robert James Terry, the





L. O. Pie M.D.



George Dock Sc.D., M.D.



Ernst F. Tiedemann M.D.

# Medical School



Philip A. Schaffer Ph.D.



Joseph Erlanger M.D.

## Faculty of the School of Medicine

only full-time member of the old faculty to be retained following Abraham Flexner's scathing review of the Medical Department of Washington University, spoke of developments which led to the new school. That afternoon, again out of doors on the lawn, Professor George Dock spoke of the relationship of the university hospital to the community. Following Dock, there was a speaker of tremendous celebrity, a hero of the day, in 1915, General William Crawford Gorgas, Surgeon-General of the United States Army. Gorgas and his men had just accomplished one of the greatest feats in the history of preventive medicine. He described their efforts in successfully eradicating the mosquito from Havana and later from the Isthmus of Panama. Thus, the elimination of malaria and yellow fever had made possible the construction of the Panama Canal, which had been completed just the year before.

At 8 p.m., an academic procession formed in Ridgely Library on the university campus and proceeded to Graham Chapel, where honorary degrees were conferred by Chancellor Hall upon, among others: Janeway, Matas, Gorgas, Flexner, Welch, Vincent and Lowell.

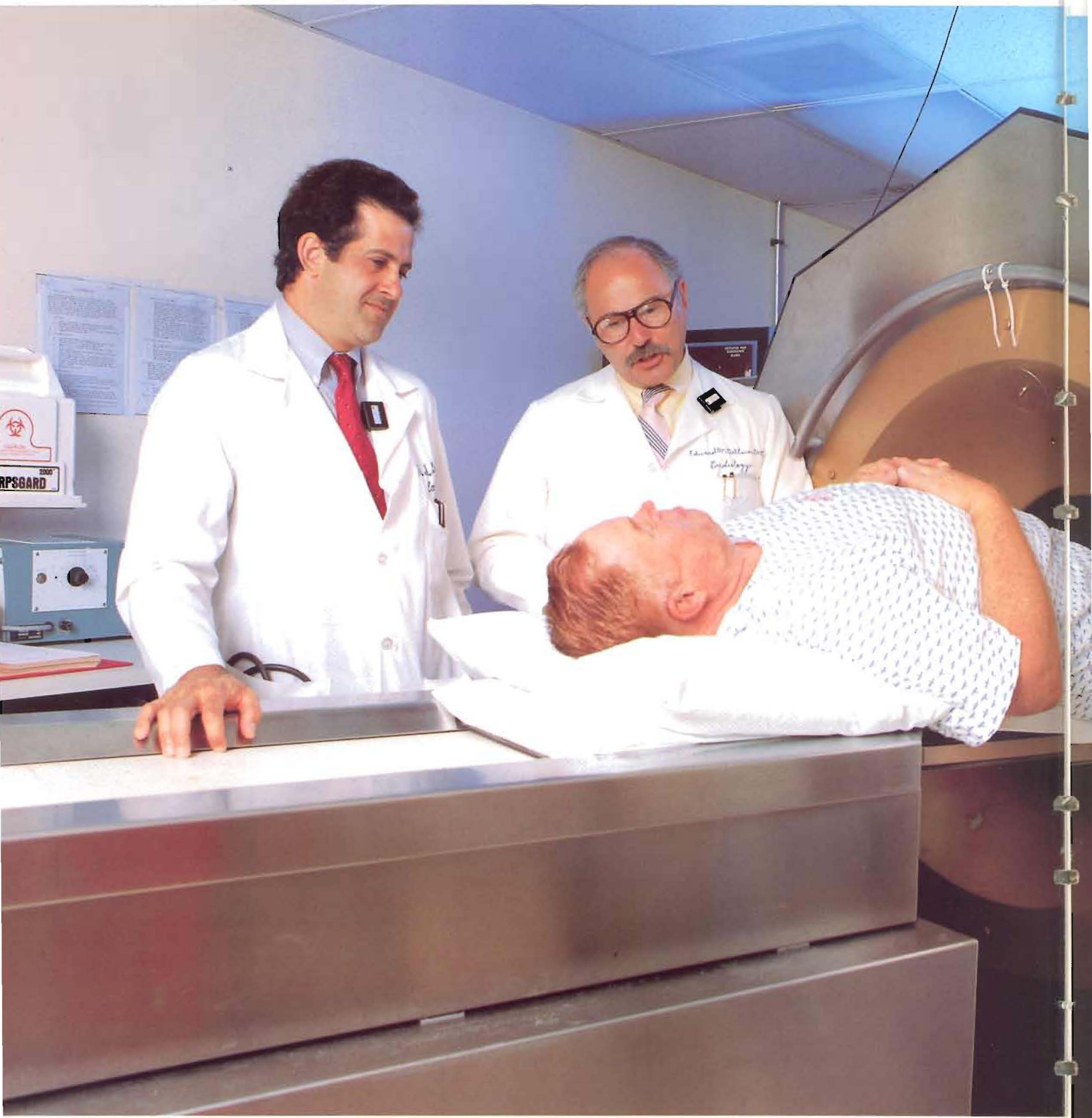
On April 28 there had been exercises held in commemoration of William Beaumont, M.D., on the occasion of the presentation of his manuscripts and letters, given by his granddaughter, Miss L. Beaumont Irwin, to the Washington University medical school. Beaumont, of course, was the army surgeon who had observed the motions of the stomach of a Canadian trapper through an opening made by a shotgun wound. The patient, young Alexis St. Martin, had been dangerously wounded by the accidental discharge of the weapon. St. Martin eventually made a complete recovery except for the permanent opening through the abdominal wall into the stomach. From 1825 through 1833, Beaumont had carried out 238 experiments on his subject, which formed the basis of his book entitled: "Experiments and Observations on the Gastric Juice and the Physiology of Digestion". During the exercises here in 1915, it was Professor Joseph Erlanger who explained the enormous impact on the world of physiology made by Beaumont in 1833. Erlanger pointed out that 70 years after Beaumont's book Osler had characterized him as "the pioneer physiologist of this

country, the first to make an important and enduring contribution to this science." Twenty-nine years later, in 1944, Joseph Erlanger and Herbert Gasser, M.D., received the Nobel Prize for their work in the South Building on the conduction of impulses by nerves.

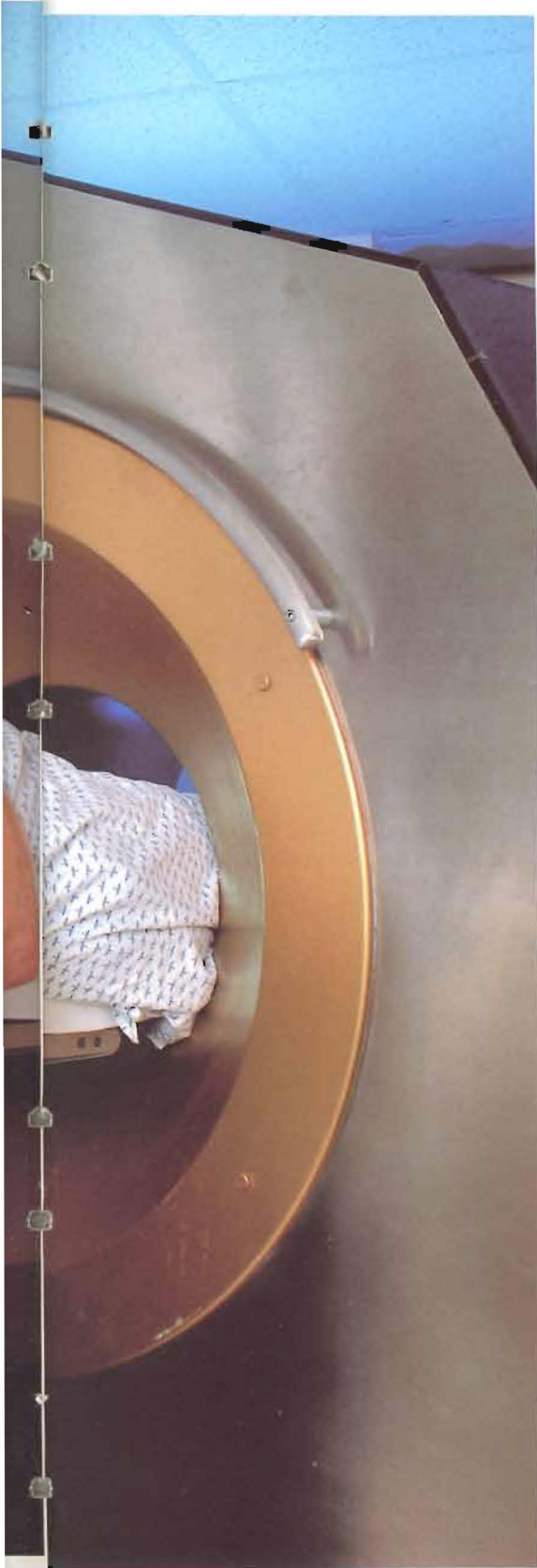
There were, of course, distinguished invitees to the ceremonies who were unable to attend. William Osler, Regius Professor of Medicine at Oxford, wrote to send his warmest congratulations but stated he could not attend because of the war.

Three-quarters of a century later, those of us working at the Washington University School of Medicine in 1990 can look back with great satisfaction upon the accomplishments of the physicians and scientists who have worked here. Gerty and Carl Cori were awarded the Nobel Prize in 1947 for their investigation, in the South Building, of the cycle which is required to change glucose into glycogen and back. Those men, in 1915, had looked forward with hope and great expectations. Similarly, we can look back with tremendous pride. Biomedical science continues today at the laboratory bench in the North, South and West buildings. Given the tremendous progress the school has made in this century, we can anticipate great accomplishments from it in the century just around the corner. ■









# PET:

*Straight from the heart*

B Y K A T H Y H E I N E

*Cardiologists Steven R. Bergmann, M.D., Ph.D., (left) and Edward M. Geltman, M.D., use PET to view the heart's metabolism. PET promises to shed new light on heart problems that have puzzled cardiologists for a long time.*



If it leaks, replace it. If it's clogged, force it open. If it doesn't work at all, get a new one.

Sounds like good plumbing advice, but also it's been the thinking behind many phenomenal advances in modern cardiology.

Valve replacement therapy, bypass surgery, balloon angioplasty, transplantation — these therapies all treat the heart on a structural level, as a pump, according to Burton E. Sobel, M.D., Tobias and Hortense Lewin Professor of Cardiovascular Diseases.

But because the heart is not made of stone or plastic or steel, but of living cells — each with a tiny structure of its own — the heart cannot always be fixed by repairing its anatomical plumbing. Sudden death and certain chronic disorders of the heart muscle, for example, do not appear to be associated with any obvious anatomical defects and may have more to do with the heart cells themselves.

They could be starved for blood or running low on fuels ordinarily carried in the blood. Or the cells may be unable to metabolize these fuels.

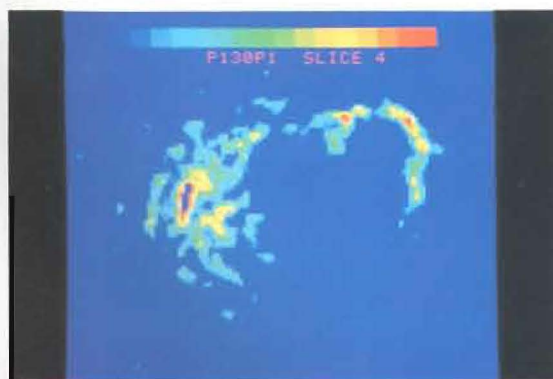
Until recently, cardiologists could not study such metabolic problems without snipping, or biopsying, pieces from the heart. But now researchers at the School of Medicine are using a new method that places the whole heart in a test tube, so-to-speak, without disturbing a single cell.

The new method, called positron emission tomography, or PET, produces images of the heart by detecting radioactively labeled molecules as they are used by the heart. Patients and research subjects who undergo PET are injected with these tracer molecules and placed in a doughnut-shaped machine that detects radioactive decay in three dimensions. Then, by completely automated number crunching, computers transform this raw data into a series of 3-D images that resemble topographical maps. But instead of mapping geographical highs and lows, PET maps the highs and lows of blood flow and metabolism.

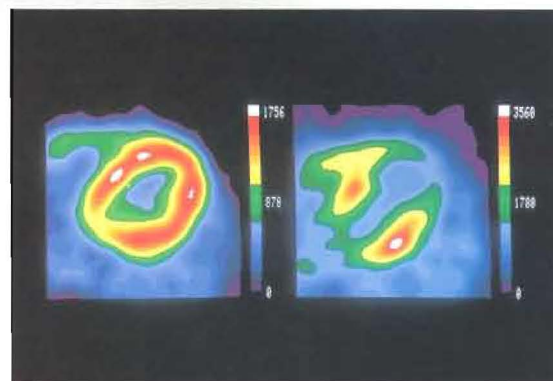
By reading these maps, cardiologists can pinpoint areas within the heart that may be injured, dead or functioning abnormally. They can also predict whether these areas can recover and how to enhance this recovery. "The promise is that disorders of the heart muscle that have remained cryptic and difficult to fathom can now be, theoretically at least, plumbed and better understood and, ultimately, better treated," Sobel explains.

Because the tracer molecules used in

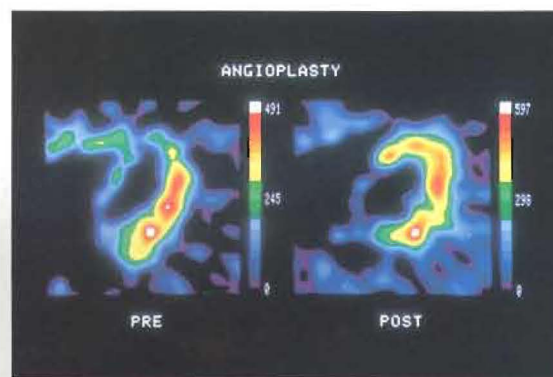
A positron emission tomography (PET) scan obtained from a patient with cardiomyopathy. In this and all subsequent figures, the images are displayed as if the body was cut transversely. Uptake of carbon-11 palmitate in patients with cardiomyopathy is non-uniform, indicative of regional heterogeneity in fatty acid metabolism. The liver, which also uses fatty acids, can be seen to the left in this image.



Transverse myocardial images obtained from a normal human volunteer (left) and a patient with an acute myocardial infarction (right). The right image shows that the effected anterior myocardium, deprived of its blood supply, has diminished oxygen consumption. Sequential scans may be used to evaluate the effects of interventional therapies on myocardial metabolism.



Transverse myocardial tomograms obtained from a patient with coronary artery disease before (left) and after (right) coronary angioplasty. These images were obtained after the administration of oxygen-15 labeled water which permits estimation of myocardial perfusion (blood flow). Perfusion is restored after angioplasty (right).



PET are chemically indistinguishable (except for their radiolabels) from substances that the heart metabolizes every day, PET does not disturb the heart's normal physiology like dyes and other foreign tracers might. Instead, it provides cardiologists with a front-row seat to the heart's biochemistry.

What the cardiologist sees depends on the type of tracer that's used. Radioactively

labeled glucose, for instance, will show how the heart breaks down sugar. A radio-labeled fatty acid, on the other hand, will reveal a picture of fatty acid metabolism.

Washington University cardiologists first began to use PET about 13 years ago to measure the amount of dead tissue left behind after heart attacks. They wanted to know whether the size of infarcts — areas



of dead tissue that arise when an area of the heart is cut off from its blood supply — had anything to do with their patients' chances for recovery.

PET gave them the answer. Using carbon 11-labeled palmitate — a fatty acid that is rapidly taken up by heart tissues and converted into carbon dioxide and water — they were able to measure the extent of these infarcts. Because damaged, or infarcted, tissues did not absorb or metabolize the radiolabeled palmitate like their healthy counterparts, infarcts appeared dark in contrast with the hot, bright, tracer-laden regions of healthy tissues. So by imaging the uptake and depletion of this physiological tracer and comparing the images with patient outcomes, School of Medicine cardiologists were able to conclude that patients with larger infarcts do not recover as well as patients with smaller infarcts.

PET also helped gain the widespread acceptance of thrombolytic therapy in which the victims of heart attacks are treated with clot-bursting drugs that open up the coronary arteries and return blood flow to the heart. Armed with PET images taken before and after thrombolytic therapy, Washington University cardiologists demonstrated conclusively that forcing open the coronary arteries with clot-dissolving drugs spares heart muscle. These studies won over many skeptics, helping to entrench thrombolytic therapy as a front-line therapy for heart attacks.

More recent PET studies by Steven R. Bergmann, M.D., Ph.D. and Edward M. Geltman, M.D. have further elucidated the recovery process that occurs after thrombolytic therapy. Using radiolabeled water as a tracer for blood flow and carbon 11-labeled acetate as a tracer for oxygen metabolism, these associate professors of medicine have learned that the return of normal blood flow is the first manifestation of the heart's road to recovery. But for the heart to completely recover normal functions, it must first resume normal oxygen metabolism — a process that takes about a week.

Bergmann and Geltman are now using PET to see if they can somehow speed up the recovery of normal oxygen metabolism by administering certain drugs in conjunction with the clot-dissolving drugs t-PA and streptokinase. PET may not only prove invaluable in evaluating the effectiveness of these and other new drugs, but also may prove useful in evaluating the need for and the effectiveness of clinical procedures such as bypass surgery and angioplasty (a procedure in which blood vessels are opened up with a balloon-like device).

Geltman and Robert J. Gropler, M.D., an instructor in radiology, are now investigating whether or not they can use PET to predict the likelihood of heart tissue recovery after angioplasty or bypass surgery in angina patients. It is difficult, if not impossible, to make such predictions using any other currently available diagnostic techniques, according to Geltman.

He and Gropler hypothesize that, although stunned heart muscle can survive short periods of time without oxygen (through anaerobic metabolism), it cannot live indefinitely without this vital nutrient.

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**"The promise is that disorders of the heart muscle that have remained cryptic and difficult to fathom can now be, theoretically at least, plumbed and better understood and, ultimately, better treated," Sobel explains.**

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Geltman and Gropler can use PET to measure the ratio of oxygen metabolism to non-oxygen metabolism, which they believe may be the best predictor of heart muscle recovery.

Beyond PET's evaluative and predictive uses, PET promises to shed new light on heart problems that have puzzled cardiologists for a long time. PET offers new hope for heart transplant patients who, for reasons unknown, tend to develop an accelerated version of coronary artery disease. "Some people get hearts from very young adults. Yet five years later these hearts look like the hearts of 80-year-olds, and may even require retransplantation," says Bergmann.

As a result, all heart transplant recipients must frequently undergo coronary catheterization to monitor them for coronary artery disease. This procedure is invasive and not without risk.

Bergmann and Geltman are now working with Sobel, Edward T.A. Fry, M.D., and cardiology fellow Martha J. Senhoff, M.D., to see if they can use PET to detect blood flow problems in the heart as soon as they start. And they are also using PET to explore why transplant patients experience this problem in the first place. Says Sobel, "Cardiac PET may be important in defining

the mechanisms of the ultimate failure of transplants in some patients, while protecting individual patients against such failures by identifying them early."

PET also promises to be important in the diagnosis and treatment of people with syndrome X — a condition in which patients experience the chest pains and shortness of breath that typifies coronary artery disease, yet their arteries show no signs of narrowing when they undergo coronary catheterization.

By monitoring these patients' blood flow under a drug-induced state that mimics exercise, Bergmann has discovered that roughly half of these people are unable to increase the blood flow to their heart muscle. "There must be some intrinsic defect that interferes with their ability to raise blood flow for normal everyday activities like walking up the stairs," Bergmann says. "The next step is to use PET to evaluate a number of drugs that we feel may be beneficial to these people."

Sobel is especially excited about PET's ability to distinguish between heart muscle disorders that are caused by coronary artery disease and those associated with other problems such as muscular dystrophy, chronic alcohol abuse, or infectious processes. Under PET, heart muscle disorders that are caused by coronary artery disease show a patchy distribution of carbon 11-labeled palmitate, while heart muscle disorders caused by other problems show a homogeneous uptake and removal of this tracer.

It is significant that these heart muscle disorders are symptomatically similar yet yield different PET images. Being able to tell the difference between these problems is important clinically because heart muscle disorders caused by coronary artery disease are treated differently from other heart muscle disorders. Bypass surgery, for example, might help in the case of a coronary-artery-disease-induced disorder, but would not be much help for a disorder attributable to alcohol.

"Just the fact that we can look at two hearts with the same dimensions and pumping impairment and see that they are very different metabolically is a very big step forward," Sobel says. "PET's endpoints are not anatomic. The important questions are not only — is the valve working better, is the hole in the septum fixed, or is the coronary artery opened up — but rather — does the heart muscle behave normally from a metabolic point of view, and is the microvasculature behaving more normally in terms of delivering blood flow on a cell-to-cell basis?" he says. "We really have no other way to answer these questions." ■



# GENE DETECTIVES

BY ROBERT LOWES

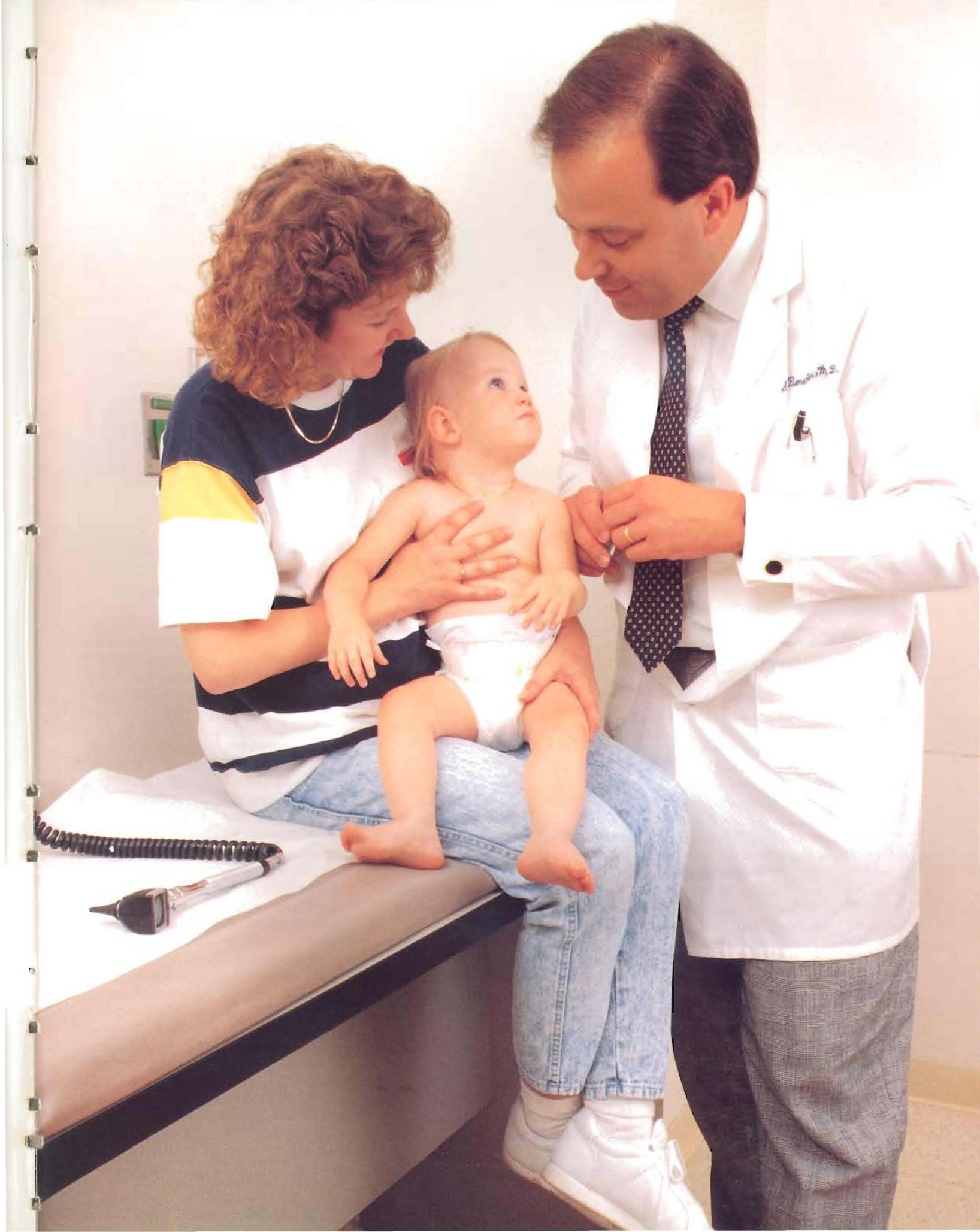
*M*ost babies can roll over by the time they're four or five months old. Katrina Becker couldn't until her seventh month.

That was one of the first clues.

The blond-haired, blue-eyed daughter of Rose and Erwin Becker, a St. Louis area couple, reached other developmental milestones somewhat behind schedule — crawling, sitting, standing. And she didn't smile much. The Beckers sent their listless, frail-looking child to a physical therapist for her poor muscle tone, but their anxieties persisted. Why wasn't Katrina progressing like other children?

*Rose Becker, Katrina Becker and  
S. Bruce Dowton, M.D.*









*The Possum (Pictures of Standard Syndromes and Undiagnosed Malformations) computer catalogues more than 1,000 diseases, listing likely diagnoses and illustrating them with any of 25,000 photographs and video clips.*

Then in December 1989, her pediatrician told the Beckers that Katrina's urine contained massive amounts of methylmalonic acid. Katrina was referred to the Medical Genetics Division of Children's Hospital, part of the Washington University Medical Center. The little girl became one of the 1,000 patients seen each year by these medical detectives who decipher diseases in the alphabet soup of human chromosomes.

The chief detective, S. Bruce Dowton, M.D., director of the division, called the Beckers in early February and said he had pinpointed the cause of Katrina's slow development. Come to my office without Katrina, he said. Tomorrow. The urgent instruction further deepened the Becker's fears, which now involved yet another life — Rose was two months pregnant.

The next day, the Australian-born Dowton told the Beckers that Katrina had methylmalonic aciduria, a genetic disorder that impaired her ability to break down four amino acids. As a result, methylmalonic acid had built up in her body, affecting brain centers in charge of muscle tone and coordination. Rose and Erwin each carried a recessive gene for the disease, but they themselves did not suffer from it. Katrina had inherited one gene

from each parent, giving her the prerequisite pair to upset her metabolism.

The odds of that happening were about one in 50,000.

**T**he odds of Katrina living an active, normal life are anything but a long shot, however, thanks to dietary therapy and vitamin B-12 injections. For Dowton, Katrina's story is one of many bright spots in the growing, but still baffling, field of medical genetics. More severe and sometimes fatal genetic diseases leave parents questioning whether life — or God — is fair. Cystic fibrosis clogs the lungs with thick mucus. Duchenne's muscular dystrophy ravages skeletal muscle. Down's syndrome produces severe mental retardation.

Researchers have identified approximately 2,000 genetic disorders, some so rare that less than a dozen cases may appear in medical literature. Dowton's challenge is identifying these maladies in patients, some of them adults, who come to the Medical Genetics Division from all over the Midwest. To gather clues, he and his staff ponder the details of a patient's appearance, analyze the DNA with genetically-engineered probes, peer through

microscopes, search a computer data base and correspond with physicians around the world who have treated similar cases.

"Because individual diseases are often quite rare, we're forced to cast a very wide net," says Dowton, an assistant professor of genetics as well as pediatrics at the School of Medicine.

The work of the Medical Genetics Division doesn't stop at diagnosis. Parents are counseled about the long-term care and treatment of their children as well as prospects of future children inheriting a disorder. Dowton's staff steers families through the health-care maze to other physicians and institutions that specialize in a given illness. Parents of affected children also need psychological healing and hope, and Dowton, a father of two, is ready to offer that as well.

"His personal commitment and caring have really made things a lot easier for us," says Erwin Becker, a metallurgist with Cerro Copper Products Co. in St. Louis.

On any given day, Dowton may see patients with defective hearts, osteoporosis, renal dysfunction, astigmatism or deafness. The specialty of genetic medicine turns its practitioners into generalists, Dowton says in his down-under accent. "I happen to like it."



**T**he Medical Genetics Division encompasses all congenital disorders, some of which can't be blamed on a recognizably faulty DNA blueprint. In some cases, the cause of cleft palate and club foot, for example, is multifactorial in nature.

"Genetic and congenital diseases are now the most common causes of death in the first year of life," says Dowton. "They have actually overtaken premature birth as a cause of death. That simply reflects that neonatal techniques are so much improved now to keep very small babies growing."

"About 3 percent of all children born will have a genetic or congenital disease that will require medical intervention. That's much higher than most people realize."

Genetic diseases originate in the 23 pairs of human chromosomes. Each chromosome is a framework for thousands of DNA-bearing genes that produce proteins and chemicals governing everything from intelligence to eye color. Nature can scramble the genetic code in any number of ways. Add an extra chromosome to a pair and the result is a trisomic syndrome such as Down's syndrome. When one of the two chromosomes in a set is missing, you have a monosomic syndrome such as Turner's syndrome, which causes short stature in females. Other diseases stem from a chromosome lacking an individual gene or a set of genes. Or a gene may be in the wrong spot on the chromosome, or in the right spot, but in a mutated form.

Diagnosis of a possible genetic disorder begins with a complete medical history and an examination that focuses on many physical features including details such as the distance between the nose and the upper lip, the shape of the ear and the texture of the hair. No single feature announces the existence of a genetic problem; rather, Dowton is looking for a constellation of unusual features. By itself, fine, sparse hair is not cause for alarm, but together with cone-shaped teeth, prominent lips and a low nasal bridge, it may signal a form of ectodermal dysplasia, whose victims cannot sweat.

Biochemical diagnostics also yields valuable clues. The Medical Genetics Division subjects urine, blood and spinal fluid samples, for instance, to gas chromatography and mass spectrometry. These procedures can identify compounds — such as methylmalonic acid in the case of Katrina Becker — that have built up in body fluids due to metabolism gone haywire.

Cytogenetic diagnostics lets Dowton's staff study culpable chromosomes directly. A blood or skin sample from the patient is grown in a tissue culture. The chromosomes are then isolated and examined under a high-powered microscope. This technique allows a geneticist to spot an obvious anomaly such as an extra chromosome. Or the geneticist might see a crimp in the sex-determining X chromosome, which gives the name to the fragile X syndrome, a common cause of mental retardation in boys.

But to fine-tune genetic diagnoses, you need to study not only individual chromosomes, but individual genes and their locations on chromosomes. Recently devel-



***Counseling plays a major role in the hundreds of consultations performed each year by Dowton.***

oped DNA probes make this possible. The probe itself is a section of a normal chromosome cloned in large quantities from bacteria.

"You're looking for the probe to bind to its complementary sequence in the person's genes," says Dowton. If a patient lacks a single gene or group of genes, "the binding will not occur." DNA probes can even map segments of an individual gene — valuable information for Dowton since the same gene can cause more than one illness, depending upon the mutation. This power of differentiation allows geneticists to distinguish Duchenne's muscular dystrophy from a milder version — born of the same gene — called Becker's muscular dystrophy.

DNA probes, which have recently helped researchers track down individual

genes responsible for cystic fibrosis, colon cancer, polycystic kidney disease and neurofibromatosis, for example, will prove instrumental in the Human Genome Project. This \$3 billion effort by the federal National Institutes of Health and the Department of Energy aims to pinpoint the chromosomal locus of each of our 100,000 or so genes. "We will attain benefits from that when disease-specific genes are located and characterized," says Dowton. "We will be able to utilize that information to help families with diagnoses."

**D**owton has yet another high-tech weapon in his diagnostic arsenal — a computer data base called Possum, or Pictures of Standard Syndromes and Undiagnosed Malformations. It catalogues more than 1,000 diseases discussed in 1,667 published cases and 1,528 clinical cases. Tell Possum facts about an unconfirmed case and the program will list likely diagnoses and illustrate them with any of 25,000 photographs and video clips on a television screen.

Nancy Mendelsohn, M.D., one of three genetics fellows in the division, recently demonstrated how smart Possum is. She called up an exhaustive checklist of physical traits. For the category of face shape, Mendelsohn checked off "flat." For the region around the eyes: "up-slanting." For the location and orientation of the ears: "low set." After entering a few more traits, she entered a command for possible diagnoses. Heading the list was trisomy 21, or Down's syndrome.

Sometimes the Medical Genetics Division refers cases to similar groups across the country that test for particular syndromes. Dowton recently coordinated blood testing for one child with investigators at Queens College in Kingston, Ontario, who work with the gene for Pelizaeus Merbacher, a syndrome that unhinges muscular coordination. Dowton's division itself attracts cases as a specialty center. Neurofibromatosis, which spawns benign tumors, is the domain of Chin-To Fong, M.D. Berengere De Martinville, M.D., studies muscular dystrophy while Michael S. Watson, Ph.D., has made fragile X syndrome his niche.

Some diseases are triggered only when a child inherits a pair of flawed chromosomes, one from each parent. Fragile X syndrome, however, can strike when just one crimped X chromosome is present (every male has at least one feminine X



chromosome in addition to a masculine Y chromosome; females have two Xs).

"There can be males carrying the (damaged chromosome) who are unaffected, which is unusual for a genetic disorder of this kind," says Watson. "That's one of the mysteries."

**T**wo months after their initial visit, the Beckers once again were seated in a waiting room at the Medical Genetics Division. Katrina, looking chipper, was pulling herself along from Mom's knees to Dad's knees and back again.

"Her energy level is much higher," Erwin told Dowton and Mendelsohn. "Her ability to walk around has really improved."

Rose, now three months pregnant, also was pleased with Katrina's progress, but she voiced worry that her next child would suffer from methylmalonic aciduria.

"With the new one," Dowton said, smiling, "there's a one-in-four chance. But turn it around. You have a three-out-of-four chance the child will be normal."

"I know you can't give me a guarantee," said Rose, her hands clutched together, "but I'm so anxious to find out."

Parents are understandably anxious when a bad gene afflicts one child and casts a shadow on the rest of their reproductive future. Dowton has seen the whole gamut of responses — sadness, guilt, denial, anger.

"They often displace that anger on the medical care system, and we attempt to absorb and understand how individuals in this situation feel and react," Dowton says. "They're unable to deal with the fact they don't have a perfect child. Every parent wants to have a perfect child."

While a few consider putting a seriously stricken child up for adoption, most families rally around their offspring. "I never cease to be amazed how well parents deal with this," says Dowton.

Rose and Erwin Becker have already made up their minds about the child whom Rose is carrying. Both Roman Catholics, they intend to forgo prenatal diagnosis and bring forth the new life no matter what. But genetic medicine already has served them well. Man's ability to crack the genetic code has restored hope for their daughter Katrina.

"We're grateful that the knowledge is there so her condition can be treated," says Erwin Becker. "We don't know what the future's going to hold, but right now, things are going very well."

Parents counseled at the Medical Genetics Division ask very common-sense questions, says Dowton. Will they walk? Will they talk? Will they go to college? Will they require surgery at some point? For a few children like Katrina Becker, the prospects of a near-normal life are very promising. A low-protein diet including special synthetic proteins reduces her intake of the four amino acids that she metabolizes poorly. Injections of vitamin B-12 improve her ability to break down whatever she does ingest. Dietary therapy also works wonders for a more widespread enzyme abnormality called PKU, or phenylketonuria, that left untreated can lead to mental retardation.

With most genetic disorders, however, the only comforts offered by a diagnosis

■  
**"About 3 percent of all children born will have a genetic or congenital disease that will require medical intervention. That's much higher than most people realize."**  
■

are damage control and realistic expectations. Children with fragile X syndrome are likely to struggle with language skills, says Watson. If you concentrate on those skills at an early age, "you can make them more educable." Parents of a child with Bloom syndrome, common among Ashkenazic Jews, know that he has a one-in-four chance of developing malignancies.

**W**hether they shorten life or shrink its horizon, genetic diseases break hearts. The worst advice you can give to families in such straits, says Dowton, is "get on with your life...have another child...time will make it all better."

"People have to be given time to deal with the situation, to grieve appropriately," he says. "The loss is always there. It won't go away, but as time goes by, it will assume the correct place in the family's life. If they don't accept it, it is often because they haven't allowed themselves a chance to grieve."

Sometimes parents ask Dowton if he can cure a disease by replacing a bad gene

with a good one. Twenty years ago, that question wasn't taken seriously. Today, with recombinant DNA techniques, correcting a person's genetic code could be around the corner. Last March, an NIH committee approved a proposal to treat children with a hereditary immune deficiency by inserting normal genes into their blood cells. These children lack a gene responsible for T-cell production of an enzyme called adenosine deaminase, or ADA. The absence of ADA causes a proliferation of toxins that destroy the immune system.

This condition is popularly known as the "bubble boy" syndrome, referring to an ADA-deficient boy in Texas who lived inside a sterile plastic tent to avoid infection. Researchers want to insert an ADA-producing gene, derived from a harmless mouse leukemia virus, into a patient's T-cells. The experimental therapy must clear several more NIH committees as well as the FDA before clinical trials begin.

Dowton applauds this government-financed venture into gene therapy, but he also urges the government to increase funding for current testing and treatment programs. Frequently, they're not covered by health insurance policies. When coverage is available, reimbursements tend to be inadequate, says Dowton, because they're skewed toward medicine by procedure, not long hours of counseling parents, studying photographs, reading medical literature, corresponding with physicians and head-scratching.

"A lot of what we do as geneticists is intellectually based time," says Dowton.

The Medical Genetics Division at Children's Hospital already benefits from some government largesse — specifically, grants from the states of Missouri and Illinois and the City of St. Louis. Dowton is actively lobbying for more public underwriting.

Government must also step in to help resolve several ethical issues confronting genetic medicine, according to Dowton. Some observers fear that advanced diagnostics will spawn a "biological underclass" of individuals whose genes reveal problematic medical futures from day one. Insurance companies may deny them coverage for "pre-existing conditions" or force them to pay excessive premiums. Discrimination could extend to the job market. Employers might be leery of hiring or promoting someone predisposed to a heart attack at age 45.

"I think these are serious questions society will be forced to face," says Dowton. ■



## Match Day 1990

A total of 113 students were graduated from the School of Medicine earlier this summer. Through the National Residency Matching Program, 83 percent of these graduates matched with one of their top three choices for post-graduate clinical training. Sixty-three percent matched with their number one choice, an increase over last year.

Internal medicine residencies were most popular among the graduates. General surgery and pediatrics were also leading selections. Seventy-two of the 113 participants selected one of these three fields.

Forty-five of the new physicians are staying in Missouri for their post-graduate training, most of them at Washington University Medical Center hospitals. Other states frequently selected are California: 12; Illinois: 6; Pennsylvania: 6; and Massachusetts: 5.

### California

#### Los Angeles

Cedars Sinai Medical Center  
Michael G. Ridgeway,  
General Surgery  
Scott E. Silverman, Internal  
Medicine Preliminary,  
University of Southern  
California, Ophthalmology  
Steven R. Stolz, General  
Surgery

Harbor-UCLA Medical  
Center

Iris Wagman Borowsky,  
Pediatrics

VAMC West Los Angeles  
Ian Yip, Internal Medicine  
*Oakland*

Kaiser Permanente Medical  
Center

Andreas E. Heller, General  
Surgery

#### Pasadena

Huntington Memorial  
Hospital

Jeanne C. Tsai, Internal  
Medicine

#### San Diego

Mercy Hospital

Maki C. Goskovicz,  
Transitional

University of California San  
Diego Medical Center

Thomas R. McMinn,  
Internal Medicine

#### Stanford

Stanford Affiliated Hospitals

George G. Gibbs, Internal  
Medicine

Robert M. Jasmer, Internal  
Medicine

Carl Y. Owada, Pediatrics

### Colorado

#### Denver

University of Colorado  
School of Medicine

Gladys A. Richardson,  
Family Practice

Thomas R. Vendegna,  
Internal Medicine

### Connecticut

#### New Haven

Yale-New Haven Hospital

David W. Drucker, Internal  
Medicine



On Match Day: Peter Apicella (left), Mitchell Fremling and Gyan Brard.





*Steven Kane and Marianne Sweetser.*

Leigh V. Evans, General  
Surgery  
Yale/Waterbury Hospital  
Neil J. Silverman, Internal  
Medicine Preliminary

**Illinois**  
*Belleville*  
Scott Air Force Base  
Paul L. Dassow, Family  
Practice  
*Chicago*  
Children's Memorial Hospital  
Kirsten M. Baker, Pediatrics  
Paul A. Miller, Pediatrics  
University of Chicago  
Hospital

Gregory R. Cizek,  
Radiology - Diagnostic  
University of Illinois Hospital  
Evan K. Saunders,  
Obstetrics & Gynecology

*Oak Park*  
West Suburban Hospital  
Center

Warren K. Slaten,  
Transitional, UMDNJ-  
New Jersey Medical  
School, Physical Medicine

**Indiana**  
*Bloomington*  
Indiana University Medical  
Center  
Jeffery D. Grills, Pediatrics

**Kentucky**  
*Louisville*  
University of Louisville  
School of Medicine  
Mary R. Morgan, Pediatrics

**Kansas**  
*Kansas City*  
University of Kansas Medical  
Center  
Gyan S. Brard, Internal  
Medicine

**Maryland**  
*Baltimore*

John Hopkins Hospital  
Cristina M. Petit, Obstetrics  
& Gynecology  
Cornelius J. Clancy, School  
of Hygiene and Public  
Health, Research-Clinical  
Medicine

Sinai Hospital  
Benjamin Movsas, Internal  
Medicine Preliminary,  
Johns Hopkins Hospital,  
Radiology - Diagnostic  
University of Maryland  
Edward D. King, General  
Surgery, Urology

*Bethesda*  
Bethesda Naval Hospital  
John L. Lindsey,  
Transitional

## **Massachusetts**

### *Boston*

Brigham & Womens Hospital  
Roger C. Inhorn, Internal  
Medicine

Bradley J. Quade, Pathology  
Edwin K. Silverman,  
Internal Medicine

Children's Hospital  
Victoria R. Masakowski,  
Pediatrics

### *Cambridge*

Mount Auburn Hospital  
Justin F. Thulin, Internal  
Medicine Preliminary

## **Michigan**

### *Ann Arbor*

University of Michigan  
Hospitals

Michael N. Polinsky,  
Neurosurgery

### *Detroit*

Wayne State University,  
Detroit Medical Center  
Dexter E. Arrington,  
Obstetrics & Gynecology

### *Royal Oak*

William Beaumont Hospital  
James K. Bischoff, Surgery  
Preliminary, Washington  
University, Otolaryngology

### *Ypsilanti*

CMHC/St. John's Mercy  
Hospital

Anthony T. Pu, Internal  
Medicine Preliminary,  
University of Michigan,  
Radiation Oncology

## **Minnesota**

### *Minneapolis*

Hennepin County Medical  
Center

David L. Bowlin, Internal  
Medicine

### *Rochester*

Mayo Graduate School of  
Medicine

Nancy M. Lynch,  
Orthopedic Surgery

## **Missouri**

### *Columbia*

University of Missouri  
Hospital



Anita J. Holtz, Family Practice  
*St. Louis*  
 Deaconess Hospital  
 William S. Anast, Internal Medicine Preliminary, University of Missouri, Anesthesiology  
 St. John's Mercy Medical Center  
 Shahrdad Khodamoradi, Transitional, Washington University School of Medicine, Radiation Oncology  
 St. Mary's Health Center  
 Christopher D. Newell, Internal Medicine Preliminary, Barnes Hospital, Anesthesiology

Washington University Medical Center  
 Barnes Hospital  
 Todd D. Alexander, Surgery Preliminary  
 Steven E. Collum, Anatomic Pathology  
 Michael P. Curran, Orthopedic Surgery  
 Steven M. Fine, Internal Medicine  
 Mitchell A. Fremling, General Surgery  
 Adam J. Gerber, General Surgery, Washington University, Urology  
 Christina L. Guyton, Psychiatry  
 Curtis R. Hall, Anatomic Pathology

John O. Krause, Orthopedic Surgery  
 John G. Lacy, Anatomic Pathology  
 Hamid R. Latifi, Radiology - Diagnostic  
 Dean Y. Li, Internal Medicine Preliminary  
 Robinna Lorenz, Laboratory Medicine  
 Brent W. Miller, Internal Medicine  
 Linda R. Peterson, Internal Medicine  
 Shawn P. Quillin, Radiology - Diagnostic  
 Mary Beth Scholand, Internal Medicine  
 Leland Scott, Internal Medicine Preliminary, Johns Hopkins University, Neurology

Alistair J. Scriven, Internal Medicine  
 Christopher M. Speidel, Internal Medicine  
 Peter G. Van Deerlin, Obstetrics & Gynecology  
 Dean H. Weber, General Surgery  
 Rebecca S. Wolfer, General Surgery  
 Jewish Hospital  
 Peter L. Apicella, Radiology - Diagnostic  
 William J. Benevento, Internal Medicine Preliminary, Washington University, Ophthalmology  
 Lawrence R. Brown, Internal Medicine  
 Paul L. Chesis, Internal Medicine Preliminary



*Nancy Lynch and John Carey.*



Andy C. Dean, Internal  
Medicine Preliminary,  
Cornell University, New  
York Hospital, Neurology  
Steven A. Kane, Internal  
Medicine Preliminary,  
Columbia University/  
Harkness Eye Institute,  
Ophthalmology  
Lyree N. Mikhail, Internal  
Medicine Preliminary  
Margaret K. Poulos, Internal  
Medicine Preliminary,  
Washington University  
Medical Center,  
Ophthalmology  
William S. Schwab, Internal  
Medicine

St. Louis Children's Hospital  
Robert O. Heuckeroth,  
Pediatrics

Peter S. Keiffer, Pediatrics  
Margaret R. MacDonald,  
Pediatrics

Arun A. Rangaswami,

Pediatrics

Randall R. Sercombe,  
Pediatrics

Marianne T. Sweetser,  
Pediatrics

Washington University  
Andrew Hing, Postdoctoral  
Fellowship - Chemistry  
Albert H. Park, Research -  
Otolaryngology  
Jonathan Silverstein,  
Research - Pharmacology

#### **New Mexico**

*Albuquerque*

University of New Mexico  
School of Medicine

Peter A. Looby, Orthopedic  
Surgery

#### **New York**

*New York*

New York University Medical  
Center

David A. Russian, Internal  
Medicine

Presbyterian Hospital

Daniel S. Horwitz,  
Orthopedic Surgery



***Marcie and Frank Bellafore.***

#### *Rochester*

Strong Memorial Hospital

Brian N. Schwartz, Surgery  
Preliminary, Urology

#### **North Carolina**

*Durham*

Duke University Medical  
Center

William N. Peugh, General  
Surgery

#### **Ohio**

*Cleveland*

Cleveland Clinic Foundation

Barry T. Kahn, Surgery  
Preliminary

*Cincinnati*

University of Cincinnati  
Hospital

Betty S. McDonald,  
Pediatrics

Douglas G. Young, Internal  
Medicine

Paul J. Eastmann, Family  
Practice

#### **Pennsylvania**

*Philadelphia*

Thomas Jefferson University

Shih-Wen Hsu, Internal  
Medicine

Francis X. Keeley, Surgery  
Preliminary, Urology

Temple University Hospital

Philip N. Salen, Internal  
Medicine

University of Pennsylvania

Martin M. Matzuk,  
Pathology & Lab Medicine

*Pittsburgh*

University Health Center

Babu V. Gupta, Psychiatry  
Montefiore Hospital

Darryl L. Houston,  
Transitional, Allegheny  
General Hospital,

Anesthesiology

#### **Tennessee**

*Memphis*

Methodist Hospital

Sann R. Gossum,  
Transitional, Campbell's  
Clinic, Orthopedic Surgery

*Nashville*

Vanderbilt University Medical  
Center

Dale S. Horne, Surgery  
Preliminary, Neurosurgery

#### **Texas**

*Houston*

Baylor College of Medicine

John J. Lee, Internal  
Medicine

#### **Utah**

*Salt Lake City*

University of Utah Affiliated  
Hospitals

Jennifer A. DeBlieck,  
Internal Medicine

Timothy M. DeBlieck,  
Family Practice

#### **Virginia**

*Charlottesville*

University of Virginia

Frank J. Bellafore,  
Pathology

*Roanoke*

Roanoke Memorial Hospitals

Jerome R. Freund, Family  
Practice

#### **Washington**

*Seattle*

University of Washington  
Affiliated Hospitals

Deborah L. Greenberg,  
Internal Medicine Primary  
William T. Dauer, research  
in molecular biology

Tammy Z. Movsas, research  
fellowship

Bradley J. Snyder, will be  
taking a year off to be  
President of AMSA

# REUNION '90



*William Curtis, M.D.  
'40 (right) and John C.  
Lemon, M.D. '55.*





*Award winners (seated) Grace Bergner, M.D. '43, Lauren V. Ackerman, M.D., Dorothy Reister, M.D. '50. Standing are Maurice J. Lonsway, M.D. '50 (left), I. Jerome Flance, M.D. '35, Purnell W. Choppin, M.D. F.H.S., Robert Paine, M.D. F.H.S. and Leonard Jarett, M.D. '62.*

### *Alumni Achievement Awards:*

**Purnell W. Choppin, M.D., H.S. '57**, president of the Howard Hughes Medical Institute, is considered by colleagues to be a "humble, unassuming" man who is always willing "to put himself in a position to help others." As an intern and resident in internal medicine at the School of Medicine in the early and mid-1950s, Choppin began building a highly successful career as an investigator, administrator, teacher and physician, first at Rockefeller University and then at the Hughes Institute. He has established himself by discovering the means by which certain viruses, particularly influenza and measles viruses, penetrate cells, attack the body defense mechanisms and multiply,

research that ultimately opened up a new field of drug therapy. He was eventually named the Leon Hess Professor of Virology at Rockefeller in 1980, heading a laboratory that continues to concentrate on his initial discoveries. He has been the recipient of numerous honors and awards, and has been an adviser to various governmental and private organizations in the fields of virology, multiple sclerosis, cancer and research.

**Leonard Jarett, M.D., '62.** Leonard Jarett built the School of Medicine's Division of Laboratory Medicine into a model for the nation as its first head in 1969, and, in the early '80s, built the Department of Pathology and Laboratory Medicine at the University of Pennsylvania into one of the top three such departments in the nation. As

a researcher Jarett has concentrated in the field of insulin action, where he has made several major technological advances and seminal scientific observations that have opened new areas of research. He has had more than 129 original papers, 23 books or book chapters and 100 abstracts published. And as a professor, he has trained more than 30 individuals who are now chairmen of departments, division heads or faculty members at academic institutions throughout the world.

**Dorothy D. Reister, M.D., '50**, has fought long and hard for a variety of worthy medical causes for children and battled to help women become leaders in medicine. The longtime Kansas City pediatrician received her medical degree in 1950 and, following a year's internship at Hahnemann Hos-

pital in Philadelphia, returned to St. Louis as a resident in pediatrics at St. Louis Children's Hospital. She joined Well Baby Clinics in St. Louis County and became an instructor in pediatrics at Washington University in 1953, before moving permanently to Kansas City in 1955. She has been in private practice since 1956. She was the first woman president of the Jackson County (Missouri) Medical Society, which is now the Metropolitan Medical Society of Greater Kansas City, and will become the first woman president of the Missouri State Medical Association, after previously serving as that organization's first woman council representative and council chairman. In addition to serving on the boards of several organizations, she is past president of the American Medical Wom-



en's Association and has been a member of the American Medical Association and the Greater Kansas City Pediatric Society.

### *Alumni/Faculty Awards*

When colleagues speak of **Grace E. Bergner, M.D., '43**, they not only talk of her professional and academic acumen, they also say: "She was loved by all her patients and staff as though she were part of their families." "She has given more time caring for others than one can imagine." "Compassionate and caring. Her untiring efforts were evidence of her dedication to the field of medicine." Following her graduation from the School of Medicine, she was an intern at Barnes Hospital before becoming an assistant resident there. In 1944, she went to Yale New Haven Hospital as an assistant resident before moving to Harvard Medical School where she was the Commonwealth Fund Research Fellow in Metabolic Diseases. She returned to St. Louis in 1947 as a partner in Grant Medical Clinic, ultimately staying there for 40 years. She served on the staffs of Barnes Hospital, Missouri Baptist Hospital, and St. Luke's Hospital in St. Louis. Her academic career began in 1948 as an instructor in clinical medicine at the School of Medicine, and she became an emeritus associate professor of clinical medicine in 1987.

For more than half a century, **I. Jerome Flance, M.D., '35**, has devoted himself to the St. Louis community and to the School of Medicine. As one colleague put it, "He has

served as a role model for generations of physicians," through his varied roles as an extraordinary teacher, researcher, clinician and civic leader. After graduating from the School of Medicine in 1935, with an internship and residency at Jewish Hospital, Flance moved on to become a resident at Robert Koch Hospital, which was then the St. Louis City Tuberculosis Hospital. After three years there, Flance relocated to New York in 1940 as a resident in the Pneumonia Service at Harlem Hospital. After returning to St. Louis, he joined the School's clinical faculty, was named director of the Washington University Pulmonary Service at St. Louis City Hospital, and also became a Pulmonary Consultant to Barnes and Jewish Hospitals. In 1953, he helped initiate the Home Care Program at Jewish Hospital, serving as its director for 11 years, during which time he instituted a home care program for tuberculosis patients. It was the first such formal program in the United States and has subsequently served as a model for others. On Flance's 65th birthday in 1976, friends and patients established the I. Jerome Flance Visiting Professorship in his honor.

**Maurice J. Lonsway Jr., M.D., '50**, is an outstanding pediatrician and leader in the medical community. Following an internship at St. Louis City Hospital and residency in pediatrics at St. Louis Children's Hospital, Lonsway went to Boston as a fellow at Children's Hospital. He returned to St. Louis that same year as an instructor in clinical pediatrics at Washington University and joined the

staffs of St. Louis Children's Hospital and St. Luke's Hospital. He joined the staff of St. John's in 1956. With the help of his father, Maurice Lonsway Sr., M.D., he aided in the formation of the Children's Clinic, which resulted in a very active pediatric unit at Children's Hospital and Washington University. He has been an influential leader at Children's, serving as president of the Medical Staff twice. A full professor of clinical pediatrics since 1980, he is known for his personal attention to students and residents. He is a member of the Admissions Committee of the School and was clinical representative to the School of Medicine Executive Faculty from 1977-1981 and in 1974 was president of the St. Louis Pediatrics Society.

For over three decades, **Robert Paine, M.D.**, has consistently been a favorite of medical students. A three-time Teacher of the Year Award winner, he is also a valued member of the Department of Medicine. A 1944 graduate of Harvard Medical School, he was an intern and resident at Barnes Hospital before joining the Air Force in 1946. Following his military service, he returned to the School of Medicine as a Rockefeller Fellow in Medicine. He was named chief of the Department of Medicine and also appointed to the newly created position of coordinator of medical education at St. Luke's Hospital in 1963. He served in those positions until last year, stepping down to concentrate his efforts as director of St. Luke's Heart Institute in cardiology, a field in which he is considered an expert. He is a professor of clinical medicine at the School

of Medicine, a position that he has held since 1972.

### *Distinguished Service Award*

**Lauren V. Ackerman, M.D.**, is a medical pioneer, author, influential teacher, and an authority in surgical pathology. A 1932 graduate of the University of Rochester Medical School, Ackerman interned at the University of California at San Francisco (UCSF) before completing residencies in tuberculosis, medicine and pathology in California and Massachusetts. In 1939, he became an instructor of medicine and pathology at UCSF before joining Ellis Fischel State Cancer Hospital in Columbia, Missouri, as a pathologist and medical director for the next year. In 1942, Dr. Ackerman joined the faculty of the School of Medicine as an assistant professor of pathology while still working in Columbia. He is recognized for training an entire generation of surgical pathologists, many of whom are professors and directors of programs across the country, as well as for making Washington University Medical Center the pre-eminent center in the world in which to train in surgical pathology. In addition, he is the author of "Surgical Pathology," which is now in its seventh edition. The author of more than 185 publications, Dr. Ackerman is a highly respected consultant and lecturer. He holds innumerable national and international honors for his contributions to pathology as well as to cancer research.



*Roger L. Mell, M.D. '65 (right), president of the Washington University Medical Center Alumni Association passes the gavel to incoming president Joseph F. Ruwitch Jr., M.D. '66.*



*W. Grant Stevens, M.D. '80, (left), Bert Mandelbaum, M.D. '80 and Bill Morgan, M.D. '80.*



*Everett Jung, M.D. '55 (left) with friends.*



*William Shaw, M.D.*

Scientific program  
speaker Irving  
Selikoff, M.D.



Attendees danced to  
the music of the Hot  
Docs.



Mrs. A. Norman  
Arneson (facing  
camera) hugs  
Mrs. J. Ted Jean.



Robert A. O'Dell,  
M.D. '55 (left), Jules  
Kernan, M.D. '55,  
Wayne Buck, M.D.  
'55 and Mrs. Buck  
greet Charlie  
Ruggieri.



David Goldring, M.D. '40 (right) with Llewellyn Sale Jr., M.D. '40.



*Chancellor William  
H. Danforth, M.D.  
(left) and Leonard  
Jarett, M.D. '62.*



*James Mann, M.D.  
'40 (left) and William  
Read, M.D. '40.*



*Mildred Trotter,  
Ph.D. and Joseph  
Iwano, M.D. '50.*



*Class of 1950.*



*Miles Whitener, M.D.  
'55 (left), Fred  
Krause, M.D. '55  
and Robert Drews,  
M.D. '55.*



*Roger Fuller, M.D.  
'50 and friends.*



*William A. Peck,  
M.D., vice chancellor  
for medical affairs  
and dean (right) with  
William Berman,  
M.D. '35 and Ann  
Henrichs, M.D. '50.*





*Irving Selikoff, M.D.  
(left) and Richard  
Sutter, M.D. '35.*

*Ann Henrichs, M.D.  
'50, Shields Livingston,  
M.D. '50, Wesley  
Gabrio, M.D. '50 and  
Harriett Livingston,  
M.D. '50.*



*Everett Jung, M.D.  
'55 (facing camera)  
with friends.*



*Mrs. Richard H. McIlroy (left), Richard H.  
McIlroy, M.D. '35, V. Terrell Davis, M.D. '36,  
Evelyn Ivey-Davis and Leo Sachar, M.D. '35.*



*John Skinner, M.D.  
'40 and William Read,  
M.D. '40.*

*Edward Emura, M.D.  
'50 greeting friends.*



*Mrs. Edward Emura  
(right) with Dr. and  
Mrs. John C. Herweg.*



*Roger Fuller, M.D.  
'50 and Edward  
Emura, M.D. '50.*



*Dorothy Reister, M.D.  
'50, W. Spencer Payne,  
M.D. '50 and M.  
John Epp, M.D. '50.*



*Dean's luncheon,  
Olin residence hall.*





*Class of 1955.*



*Seymour Brown,  
M.D. '40 and  
Robert Anschuetz,  
M.D. '40.*



*Joseph Mira, M.D.,  
'40 (left) and Robert  
Garrett, M.D. '40.*



*Washington University Medical Center.*



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**WASHINGTON**

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**UNIVERSITY**

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**SCHOOL OF**

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**MEDICINE**

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AT WASHINGTON UNIVERSITY MEDICAL CENTER

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660 SOUTH EUCLID AVENUE

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CAMPUS BOX 8065

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ST. LOUIS, MISSOURI 63110

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*This spring's graduates of the School of Medicine included 92 recipients of the M.D. degree, 19 of the M.D./Ph.D. and 2 of the M.A./M.D. The School also awarded 27 degrees in health administration, 39 in physical therapy and 36 in occupational therapy.*