Eye Center Gives Kids a Fighting Chance
Long before the age of the PET scan, phrenologists believed they could map brain functions and emotions by reading the bumps on the head. The phrenology chart above is from Der Gesichtsausdruck des Menschen by Hermann Krukenberg. Stuttgart, 1913. Courtesy of the Medical Library's rare book collection.
A Personal Note on Albert Roos
This 72-year-old cell physiologist and classical pianist has no intention of retiring.

For Their Eyes Only: A Closer Look at Pediatric Ophthalmology
The new Eye Care Center at Children's Hospital provides care for children with all types of eye disorders.

Scientists Meet the Rising Sun of Medical Research
The School of Medicine enters into a unique exchange program with the Japanese life science research institute, RIKKEN.

Tracing the Senses
Improved resolution of the PET scan allows researchers to map brain function and literally trace the senses.

On the Cover:
A former patient of Fred C. Chu, M.D., at the Pediatric Ophthalmology and Eye Care Center, Ray Kube Jr. has gone on to win the St. Louis Golden Gloves Championship and first place in the regional Junior Olympics.
Faculty Join National Academy of Sciences

Two researchers from the School of Medicine have been elected to the National Academy of Sciences.

Philip Needleman, Ph.D., Alumni Professor and head of the Department of Pharmacology, and Emil R. Unanue, M.D., Edward Mallinckrodt Professor and head of the Department of Pathology, are among 61 new members honored for their distinguished and continuing achievements in original research.

Election to the academy, which now has 1,523 members, is one of the scientific community's most prestigious honors. The society, chartered by an act of Congress signed by President Lincoln in 1863, promotes research beneficial to human welfare and officially advises the federal government on science and technology.

Needleman was elected in part for his research on atriopeptins, chemicals produced in the heart that dramatically affect the kidneys and the body's internal fluid environment. Needleman's research team isolated and established the molecular structure of atriopeptins in 1983. That discovery culminated a search that had gone on several decades in the scientific community to learn the nature of an elusive factor in the blood that regulates salt and fluid balances in the body.

Needleman is also a foremost authority on prostaglandins, hormone-like substances that affect many of the body's regulatory systems. He has made specific contributions to the relationship between prostaglandins and blood clotting, blood pressure regulation and heart disease.

Needleman joined the School of Medicine faculty in 1967 as an assistant professor, and was named head of the pharmacology department in 1976. He has held the Alumni Endowed Professorship since 1982, and has been voted 'Teacher of the Year' four times by senior medical students. He received his doctorate from the University of Maryland in 1964, and served postdoctoral and advanced research fellowships at the School of Medicine.

Unanue is an immunopathologist who has centered his research on the interactions among immune system cells. He has been instrumental in showing the critical role played by macrophages, cells that activate the body's immune response to foreign invaders. Macrophages ingest and destroy foreign substances, and also stimulate the production of specific white blood cells that attack invaders. Macrophage interactions with other immune system cells are important in organ transplants, and in the body's response to many disease states, especially infection and cancer.

Unanue has been head of the School of Medicine's pathology department since 1985. He came to St. Louis from Harvard Medical School, where he had been a faculty member since 1970, and Mallinckrodt Professor of Immunopathology since 1974. He received the M.D. degree in 1960 from the University of Havana School of Medicine, and served an internship in pathology at Presbyterian University Hospital in Pittsburgh.

Growth Factors Lead to Improved Wound Healing

Surgeons may one day speed wound repair by applying the body's own healing agents in even larger quantities than the body can make them by itself.

Wound-repair studies by Thomas A. Mustoe, M.D., assistant professor of surgery, show that one such agent—a growth factor made by blood platelets—can, in sufficiently large quantities, help wounds to heal in less than half the usual amount of time.

Mustoe was turned on to the wound-healing potential of platelet derived growth factor, or PDGF, by Thomas F. Deuel, M.D., professor of medicine and biological chemistry. Deuel was first to identify and crack the genetic code for PDGF, making it easier to manufacture in large quantities.

Deuel uncovered several clues that implicated PDGF as a key player in the healing process. Its ability to stimulate cell division, for instance, could replace damaged cells with new cells at the site of a wound. And PDGF's magnet-like effect on tissue-building cells could be what causes these cells to migrate to the wound site. Furthermore, PDGF stimulates these cells to produce collagen, which aids healing by cementing together the sides of a wound.

These and other clues prompted Deuel to approach Mustoe with the idea of testing the effects of PDGF on
actual wounds. As a plastic surgeon who deals with issues of wound repair nearly every day, Mustoe was more than ready to accept the challenge.

To study the effects of PDGF on wounds, Mustoe makes equal, parallel incisions in experimental tissues. Then, applying it like toothpaste, he squeezes a mixture of collagen and PDGF into one cut and collagen alone into the other. Closing both wounds with surgical clips, Mustoe then lets the wounds heal for two days to four weeks, at which point he removes “healed” strips from the wounds and measures their strength. Wound strength is gauged with a tensometer, a device that measures the amount of force the wound strips can tolerate without breaking.

After measuring the wound strengths at various stages of healing, Mustoe found that the wounds treated with PDGF were twice as strong as those not treated with PDGF.

But before PDGF can be used in humans, it must first gain FDA approval. FDA tests would be aimed at making sure that the growth factor does not contain a dangerous virus, such as the AIDS virus. Another concern is the possibility that artificially high amounts of a naturally occurring growth factor could cause cancerous tumors. “One of the major differences between wound healing and cancer is that wound healing is an unregulated growth that shuts itself off,” Mustoe explains, “while cancer is an unregulated growth that never shuts itself off.” Mustoe believes, however, that the chance of PDGF causing tumors is almost nil, as PDGF is applied directly to the wound and not into the bloodstream or digestive system, where it would circulate throughout the body.

In addition to their work with PDGF, Mustoe and Deuel have found that another growth factor, called epidermal growth factor, speeds healing in burn and ulcer-like wounds. “We have shown that two different growth factors do indeed stimulate wound healing,” Mustoe says. “The real question, then, is whether we can show this with other growth factors. Can we find the ideal recipe for optimal wound healing? And, secondly, will this recipe be different in situations of stress?”

Mustoe and Deuel’s results are significant for a number of reasons. For one, there’s the concern over the cost of medical care. If better wound healing could shorten hospital stays by just a day or two, there would be tremendous cost savings. And growth factors could help certain patient sub-groups with significantly impaired healing: the elderly, malnourished, those on chemotherapy regimens and anyone on steroid therapy. In addition, the factors may be useful with hard-to-heal wounds such as bed sores and burns.

“There’s a lot of potential,” Mustoe says. “Realistically, what we’ve done so far is just a scratch in the surface. But I think we’re off to a good start.”

Genes and Alcohol

Recent research on the personalities and drinking behavior of adopted-away children of alcoholics suggest that alcoholics are born with personality traits that make them particularly susceptible to alcohol abuse. And alcoholics are likely to pass on this susceptibility to alcoholism to their children, even when the children are reared in normal adoptive homes.

In a recent Science article, C. Robert Cloninger, M.D., professor of psychiatry and genetics, described two high-risk personality profiles that can lead to different kinds of drinking problems. Cloninger found that some personality traits predispose people to start drinking, whereas others predispose them to become addicted afterwards. Because these different traits occur in all possible combinations, there is no single or specific personality type characteristic of all alcoholics.

One high-risk profile involves people who are extremely impulsive and exploratory (high novelty seeking), risk-taking and uninhibited (low harm avoidance), and independently self-willed and socially detached (low reward dependence). Individuals with this personality profile start drinking during adolescence or early adulthood and continue to initiate alcohol-seeking behaviors so that they are unable to abstain from alcohol entirely for long periods of time. This type of alcohol abuser often engages in other forms of antisocial behavior, such as reckless driving and bar brawls. As one might suspect, this “macho” form of alcoholism almost exclusively affects men.

The other high-risk profile, which is characteristic of most female alcoholics and some male alcoholics, involves the reverse combination of personality traits. These alcoholics are eager to
aged, such as drinking at “happy hour” with co-workers. These individuals are anxious, introverted perfectionists who find the anxiety-relieving effects of alcohol rewarding, so that they quickly become tolerant and dependent on alcohol. In contrast to alcoholics who cannot stay away from alcohol for long periods of time, but lose control once they start drinking. They often go on prolonged binges, and later feel guilty about their loss of control.

Evidence that these two personality types are inherited comes from studies of the adopted-out children of alcoholics by Cloninger and his associates in Sweden. Because these children were separated from their biological parents at an early age, Cloninger was able to show the importance of genetic factors. Home environment can also be important, but is not sufficient to cause alcoholism. Alcohol abuse in adoptive parents did not increase the risk of alcoholism in the children they reared.

In contrast, Cloninger found the adopted children of alcoholics were three times more likely to develop alcohol abuse than the other adoptees. He also found that the type of alcoholism they inherit was usually the same as that of their biological parent, with one exception. The exception is that women rarely express the macho or “male-limited” form of alcoholism.

These adoption studies have been further supported by laboratory studies that link individual differences in personality with subtle differences in brain chemistry. For example, exploratory novelty seekers are more sensitive to alcohol’s stimulatory effects because of greater sensitivity to a neurotransmitter called dopamine, which plays an important role in regulating responses to pleasurable experiences. On the other hand, alcohol also has anti-anxiety effects, which cause anxious and inhibited individuals to “lose their inhibitions.”

“Yet it appears we had misunderstood the whole issue from the beginning. It’s not what we learn versus what we inherit. We inherit how we learn.” According to Cloninger, people are born with different styles of learning—that is, differences in sensitivity to different kinds of experiences, such as punishments, rewards, novelty, as well as different kinds of drugs like alcohol. “We don’t all start out equal in the way we respond to experience,” he says. “The way we respond, however, is not fixed, but adaptive. While we are born with different styles of learning, these styles have not yet been behaviorally programmed, but rather are like computer software systems that allow us to adjust our behavior flexibly in response to our individual experience.”

People with damaged heart valves who are not candidates for open-heart surgery have a new option for treatment. Using larger versions of balloon catheters, which have been used for years to open up clogged blood vessels, cardiologists can now expand narrowed valves.

“It’s remarkable,” says Ronald Krone, associate professor of medicine. “These patients, who because of their age or other serious medical conditions are not surgical candidates, are walking out of here under their own power.”

In the first six cases performed at Jewish Hospital, the youngest patient was over the age of 70, four were in their 80s, and one was 92. All had refused surgery to correct their valve problems, or were determined to be at very high risk for valve surgery. The majority showed improvement following the new procedure, which involves threading a catheter through a major blood vessel into the narrowed heart valve. Around the catheter is a balloon—six to seven inches long—which is expanded to stretch the flaps of the valve to allow a better blood flow.

A narrowing of the valve opening, or stenosis, is caused by diseases like rheumatic fever or by an accumulation of calcium deposits as a consequence of aging. The new balloon valvuloplasty procedure is being studied as an alternative to surgery for the repair of mitral and aortic valves. In patients who can undergo surgery, the problem can be solved by replacing the narrowed valve with artificial valves, valves from pig hearts, or human valve grafts.
Studies of balloon valvuloplasty, both in this country and in France, have demonstrated the procedure to be safe and effective for at least six months. But because the procedure is new, no long-term statistics are available. Balloon valvuloplasty has been most extensively used in the United States at Beth Israel Hospital in Boston, where a research study on the technique has been in progress since mid-1985. This study applied the technique to both aortic and mitral valve stenosis (narrowing). Among the 57 patients discharged from the hospital after the aortic valve procedure, only four patients had a re-occurrence of stenosis within four to seven months. Three of the four had the procedure repeated with good results, and the fourth had the valve surgically placed in combination with coronary bypass graft surgery, also with good results.

The procedure was also successful for 25 of 27 mitral valve stenosis patients. The remaining two were not successful because of a problem with the placement of the catheter.

"This procedure is one of those happy inventions which allows us to help people who we couldn't help before," Krone says. "So far, the results are encouraging, but we won't know how good balloon valvuloplasty really is until we have some long-term studies. However, for the older people who cannot undergo surgery, we're able to give them an increased quality of life at least for the short term. And that's something important."

Guze Gets Gold Medal Award

Samuel B. Guze, M.D., vice chancellor for medical affairs and president of the Washington University Medical Center, has received the Gold Medal Award from the Society of Biological Psychiatry. He is the 20th recipient of the award since its inception in 1966.

Founded in 1945 to study the biological basis of behavior, the society established the award to honor pioneering work in the field. Guze was cited for his significant contributions to the advancement and extension of knowledge in biological psychiatry. He has been a leader in research on the genetic and psychiatric aspects of alcoholism, and has contributed to the characterization and reliable diagnosis of schizophrenia and hysteria.

Guze is the Spencer T. Olin Professor of Psychiatry and head of the Department of Psychiatry, psychiatrist-in-chief at Barnes and Children's hospitals and a consulting psychiatrist to Jewish Hospital.

He joined the School of Medicine faculty in 1951 and has been a member of the executive faculty since 1964. After receiving the M.D. degree from Washington University in 1945, Guze interned in medicine, and trained in medicine and psychiatry at Barnes Hospital and the School of Medicine.

He serves on numerous committees and boards at the local and national levels, is past chairman of the board of directors of the Association of Academic Health Centers and is currently on the Council of the Institute of Medicine of the National Academy of Sciences.

Johnson Receives Javits Award

Eugene M. Johnson Jr., Ph.D., professor of pharmacology, will conduct research for the next seven years with more than $900,000 in funding from a Javits Neuroscience Investigator Award.

For the past decade, his laboratory has studied nerve growth factor (NGF), a protein discovered in the 1950s at Washington University by Nobel Prize winners Rita Levi-Montalcini and Stanley Cohen with Viktor Hamburger.

Johnson's past studies focused on how NGF is transported in the nervous system, how it can prevent the death of neurons caused by certain drugs and the molecular mechanisms by which it prevents neurons from dying. His current work examines how NGF binds to the Schwann cell, believed to be a key cell in fostering peripheral nerve regeneration.

Johnson is the 10th Washington University faculty member to receive a Javits Award since the highly competitive awards program began in 1983.

Two Researchers Awarded NIH MERIT Status

Two School of Medicine researchers were recently awarded MERIT status from the National Institutes of Health, boosting the number of School of Medicine faculty members who have received MERIT status to a grand total of five.

MERIT (Method to Extend Research in Time) status will assure Donald C. Shreffler, Ph.D., professor of genetics, of long-term, uninterrupted financial support for his work on the genetics of the immunologic system and, more specifically, the genetic basis for organ and tissue transplant rejections.

The MERIT designation will similarly enable Emil R. Unanue, M.D., Edward Mallinckrodt Professor and head of the Department of Pathology, to investigate the interactions among immune system cells for up to five years. Unanue's work in this area also earned his recent election to the National Academy of Sciences.

MERIT status, which is attached to only a few NIH grants, recognizes scientists for superior achievement by providing up to five years of grant support without time-consuming paperwork and other delays traditionally associated with grant renewal applications.
A Personal Note on ALBERT ROOS

BY BRENDA MURPHY

If you ask Albert Roos, M.D., what led him to Washington University School of Medicine or to the research on respiration and intracellular pH that have brought him international recognition from his peers, he'll just as likely say it was a matter of chance rather than a carefully plotted choice.

But if you ask what makes him a good scientist, he'll reply with an answer that leaves little to fate. "I'm vitally interested in this work. I think about it day and night," he says.

At age 72, Roos, who is a lecturer in cell biology and physiology and an emeritus professor of anesthesiology, has no intention of retiring from the work that has occupied him since his arrival at the School of Medicine in 1946. The recipient of a Research Career Award from the National Institutes of Health in 1963, Roos recently was awarded a five-year grant to support his research through age 77.

"That's the character of a great scientist," offers Paul De Weer, M.D., Ph.D., professor of cell biology and physiology, who is Roos' long-time colleague and lab neighbor. "They don't change. Science is not a job for them. It's an attitude of constant questioning. When they hit 70, why quit? He has to be sick or out of town not to be here. He's always here."

Although Roos' research career got off to a late start—beginning at age 33—De Weer says his colleague is a "born scientist," possessing both a questioning mind and the ability to perform experiments. "The two make for a most superior scientist," De Weer says.

Roos' interest in science can be traced back to his childhood in the Netherlands. His father, Jacob, who was a veterinarian in Leiden and later chairman of the Department of Veterinary Physiology at the University of Utrecht, introduced the young Albert to the arena of scientific discussion. "Discussions at the dinner table were devoid of small talk," Roos recalls. "It was usually physiology, physics or music from the time I can remember. If you're receptive to that kind of thing, it was a very good atmosphere... By nature, I suppose I was receptive to what I was exposed to."

In Leiden, the elder Roos spent his afternoons working in the lab of Willem Einthoven, who received the Nobel Prize for Medicine and Physiology in 1924 for his discovery of the mechanism of the electrocardiogram. When he received his professorship, father Roos moved his family to Utrecht, where Albert was enrolled in the municipal gymnasium, the most rigorous course of study he would ever receive. "The hard work was done between my twelfth and eighteenth years," Roos recalls. "You were forced to learn how to study. There were no remedial courses and no electives."

Music was also part of the family diet. Roos' father was an accomplished flutist, his mother played the piano, his brother the violin. Albert began playing the piano at the age of six, and has played the piano on a daily basis ever since then—even considered a career in music. A portrait of his favorite composer, Mozart, hangs over Roos' desk; it is the only portrait in his office.

At his father's suggestion, the younger Roos began the study of medicine at the University of Utrecht and received the M.D. degree at Groningen in 1940. Albert continued his studies in Boston at his father's urging. He felt it was dangerous to remain in the country, Roos recalls. "The Nazis were a hundred miles away, across the border. His father's suspicions proved correct. Holland was invaded just six weeks after Albert Roos left the country for the safety of the United States. Jacob Roos did not survive the war.

When Roos arrived in the United States at the age of 26, he spoke rather broken English. "I remember going through a cafeteria line in New York, right after arriving, and ordering spinach, which I pronounced 'spynack,'" Roos says. "There really is no reason why it shouldn't be pronounced that way, except it isn't."

Roos was accepted as a fourth-year student at Harvard Medical School and was stationed at Massachusetts General Hospital in Boston. He can still recall examining his first patient there, "The patient spoke English, of course, and I took notes in Dutch and translated them later," he says.

During his six years in Boston, Roos was a medical intern at the Beth Israel Hospital and assistant resident at the Peter Kirkwood, Missouri.

Albert Roos practices the piano at his home in Kirkwood, Missouri.
Bent Brigham Hospital. During his time at the Massachusetts General, he met Fuller Albright, a professor at Harvard and a prominent physician. "He was the most brilliant man I've ever known. He had an almost childlike vision of how things fit together," recalls Roos, who enrolled in one of Albright's experimental courses. "He stimulated my determination to go into science."

Roos' experience at the Brigham also led him to conclude that he belonged in the laboratory rather than at the bedside. He relates one incident in particular: "I remember one day at the Brigham, just before ward rounds, when a relative of one of my patients wanted to speak to me. I told him I could not see him just then and overheard him asking the nurse—when he thought me out of earshot—'Who is that officious little guy?' She answered, 'That is the resident, Dr. Roos.'"

A request for a reprint of a paper Roos had written on the electrical axis of the heart in A-V block brought him to the School of Medicine. Robert J. Glaser, M.D. (now a member of Washington University's Board of Trustees), who had been a house staff member at the Brigham and was chief resident at Barnes Hospital, requested the reprint. He then helped Roos arrange a cardiology fellowship in the Department of Medicine with the late John R. Smith, M.D. Their work came to the attention of Harvey Lester White, then chairman of physiology, who offered Roos an instructorship in physiology.

Roos at first declined the offer. He was 33 years old, newly married and had little in the way of worldly goods. "The salary was so miserable that I felt I could not afford it," recalls Roos, who considered going into medical practice instead. But at the suggestion of his mother, who was visiting at the time, Roos decided to give the instructorship and his beloved experimental work a one-year trial. "It was a good decision. I would have made an impossible clinician," says Roos, whose "temporary" year's stay in the lab has endured for more than 40 years.

Soon after he joined the Department of Physiology, Roos was asked by Evarts A. Graham, M.D., then chairman of surgery, to head the newly created Laboratory of Thoracic Physiology. The purpose of the lab was to determine whether or not patients could withstand lung surgery. "He (Graham) over-estimated the use I could be to the surgeon in evaluating patients. But I had a lab and was not about to give it up," says Roos, who remained associated with the surgery department for 23 years. He started to study respiration—about which he had only rudimentary knowledge—and, in the process, taught himself calculus. "He needed it," De Weer explains. "It's part of his atti-

"Thinking is the most difficult thing for man. You have to force yourself to do it. It's an unusual kind of person who finds satisfaction in such a life."
most dedicated were Thomas F. Hornbein, M.D., now professor and chairman of anesthesiology at the University of Washington School of Medicine in Seattle, and Lewis J. Thomas Jr., M.D., director of Washington University’s Biomedical Computer Laboratory, who both started as medical students and worked on and off with Roos for more than a decade.

A mountain climber of international reputation, Hornbein was naturally interested in how breathing is affected by high altitude. He and Roos published a series of studies on the regulation of respiration, one of which (in cooperation with Zora J. Griffy) became a “Citation Classic” in Current Contents 25 years after its publication.

Thomas, who worked with Roos on pulmonary blood flow, mechanics and surface tension, says of Roos: “He’s intellectually demanding. He never had a closed mind. He always insisted on rigor. He was the ideal person to learn research work with.” De Weer agrees, adding, “He scares the weaklings away. Those that survive the barrage of scary tactics, he really molds them. They turn out to be superb scientists.”

For those medical students who worked with him, Roos’ questions in the lab were well-known. “When you hear a Roos question, you better hold on to your seat because there’s more coming,” De Weer says. That inability to accept incomplete answers followed Roos into the lecture hall—a place in which he did not particularly enjoy being. “He was never able to get himself to the level of the students,” Thomas says. “He never got very good evaluations from students, and he never really cared. He wanted to teach it right and rigorously. If a student asked a probing question, he loved that and would react for hours. He was a good teacher for students who were genuinely interested and involved in the material.”

Roos is happiest in the lab. “To be a good scientist, you have to work at it all the time. It’s difficult for your family to put up with,” says Roos, who is the father of two sons. A research scientist has no boss, no one to tell him when to come to work or when to leave. And when one is as demanding on oneself as Roos’ colleagues say he is, one spends a lot of time working. “Thinking is the most difficult thing for man. You have to force yourself... putting on his subject his thumbprint, unique and recognizable,” he writes. “A certain degree of immodesty, of arrogance even, is an indispensable ingredient.”

But although Roos’ work has received considerable recognition from his peers, he seems to downplay his achievements. “A scientist should consider himself successful when, looking at himself in his shaving mirror in the morning, he can truthfully say: ‘I did the best I could,’” he says. “All other forms of approval are distractions.”

Then, Roos returns to the subject of fate and says, with only the slightest twinkle in his eye: “I’d rather be a great composer than a great scientist. Not being either, I’ll accept my fate.”
A teacher, Dr. Fred C. Chu is accustomed to operating out loud. “To reach the muscles, we first pass through two very thin layers—here and here,” he says, probing near the eyes of the unconscious two-year-old girl. The anesthesiologist manipulates dials and checks monitors. The nurse preps a set of gleaming instruments. The surgical resident exposes the field with steady hands. Chu glances at the crowd around him. “Like everything else I do here,” he notes, “this is no solo act.”

But even his colleagues agree that an article about the Pediatric Ophthalmology and Eye Care Center is, by definition, an article about Dr. Chu. The center is located at Children’s Hospital, a sponsoring institution of the Washington University Medical Center. As its director, Chu is responsible for creating a national center for excellence in pediatric ophthalmology. And, over the last two years, his secret of success has been simple—treat one patient and one family at a time.

This morning, his patient is Kara, a girl with strabismus. Strabismus is a misalignment of the eyes that, if left untreated, can lead to “lazy eye,” or amblyopia—when the brain permanently “tunes out” one of the two eyes to suppress conflicting visual messages.

Although Chu operates to realign strabismic eyes on patients as young as four months, surgery is usually the last resort. “Sometimes the eyes of young children take a while to set,” he says. “They may intermittently be misaligned, but then lock into alignment spontaneously.”

If the eyes don’t align, and it’s clear that there’s decreased vision in one eye, the problem may be treated by affixing an eye patch over the good eye. This allows the weak eye to work equally hard to supply the brain with visual information. After that, glasses might help.

Chu has been observing Kara from the time she was one week old, and he’s tried the noninvasive approaches. But when Kara’s eyes stopped wandering and became fixed in a crossed position, he recommended surgery.

“We need to bring both eyes into forward alignment by altering the length of the muscles that hold them in place,” Chu explains, as he measures the proper length of suture bridge.

Forty-five minutes after making the first incision, Chu looks at the girl’s unconscious face; he looks into her eyes. For
Parents look on as Chu checks up on former patient and Golden Gloves boxing champ Ray Kube Jr. prior to his fight in the national Junior Olympics.

the first time in her short life, Kara has eyes that are at once relaxed and in alignment.

"We may not match the two fields of vision perfectly at this surgery," Chu says, as he strips off his plastic gloves. "But we can get them very close. At this point, we depend on the brain to wake up and say, 'Hey, I have two eyes!' so the two images are reconciled."

Chu walks in thoughtful silence to the waiting room. Although he has performed hundreds of eye muscle operations, he gives special attention to the post-operative meeting with parents.

When Chu enters the lounge, Kara’s father is staring out the window and rocking on his heels. Her mother is rapidly flipping through a magazine.

"It went grrrrreat!" says the surgeon, with hands stretched toward them. The couple has a thousand questions. They discuss details of the operation, Chu’s experience in similar cases and the nuts and bolts of Kara’s recovery. As Chu speaks, calm returns to Kara’s parents in almost visible waves.

It’s a tiny drama Chu plays out several times a week. “We know that people come here for more than the high-tech equipment and state-of-the-art care,” he says. “We recognize that things like understanding and accessibility are all part of what defines ‘quality care.’”

Chu tries to involve parents in most aspects of their child’s treatment. During examinations, he frequently invites parents to look through the slit-lamp microscope to observe the child’s problem firsthand. He counsels them in the low and compassionate tones of a fellow parent. He explains complex medical conditions with vivid and intelligible metaphors.

Of course, another aspect of dealing with parents is knowing when to back away. After Kara’s surgery, Chu examines Charles, a nine-year-old whose right eye has been blinded by advanced glaucoma and now has a painful, corneal ulcer. Chu speaks to Charles’ mother in a soft voice. “It may be time—I mean, we’ve talked about this before—to make some decisions.”

She knows he’s suggesting a glass eye. “Charles won’t hear of it,” she says. “No way he’ll consider it. He doesn’t want that, no.”

“Okay,” says Chu, smiling. “As long as he’s not in severe pain, there’s no urgency. But in this weakened state, the eye is prone to infection.”

“He wants to keep it. He wants that.” The doctor shrugs and closes Charles’ file. “Well, things change. Kids may make fun of him because the eye looks different, he’ll be discovering girls soon... let’s keep talking.”

Later, Chu concedes that a glass eye is probably the best resolution for Charles. “There’s no chance of restoring sight,” he says. “Until it’s removed, that eye will be nothing but a painful inconvenience. Charles and his family just need some time to get used to the idea.”

Chu’s advanced surgical skills and people-first style are the foundations for the success of the eye care center. Since 1985, when Chu came from a research post at the National Institutes of Health to become assistant professor of ophthal-
mology and pediatrics at the Washington University School of Medicine, the center has become one of the nation’s leading institutions for all aspects of pediatric ophthalmology. Patients throughout the Midwest are referred to Children’s Hospital for eye problems ranging from infantile glaucoma to BB-gun injuries.

“When we first arrived, we were seeing 10 or 12 patients per week,” Chu recalls. “Nowadays, I usually see that many in an hour.” The center currently schedules 30 to 40 patient-visits per day, three days a week. The remaining days are reserved for surgery.

“Dr. Chu has really invigorated the program here by drawing a lot of interesting cases,” says Dr. Robert Benedett, a surgical resident in pediatric ophthalmology. “He’s got such a reputation that referrals come in for difficult and rare cases as well as the routine.”

According to Benedett, Chu is as concerned with the patients’ primary care physicians as he is with the patients themselves. “When he gets a referral in,” says Benedett, “he calls the patient’s doctor right away, usually that same night, to tell him what’s going on. That sort of attention to communication, of course, only leads to more referrals.”

But Chu doesn’t see his personal reputation as superseding that of the institution. “What remains in people’s minds isn’t that they got the best care from Dr. Fred Chu,” he says. “What they remember is that Children’s Hospital, and by extension Washington University Medical Center, is the best place for such care.”

One recent referral involved Chu in a story that might end at the Olympic Games. Last January, a 15-year-old boxer named Ray “Punk” Kube came to the center complaining of impaired vision. “We knew there was something very wrong,” says Ray Kube Sr., the boy’s father and trainer. “Punk was walking right into punches, taking shots he’s never taken before.”

The younger Kube (rhymes with ruby) remembers seeing two of everything: “Two opponents in the ring, two punches coming at me . . . it really threw me off.”

Chu traced the problem to a paralyzed muscle in Kube’s right eye. A blow to the head probably caused the damage. “The eye has six muscles pulling at it like tethers,” the surgeon explains. “With one of those not functioning, Ray’s right eye was positioned slightly higher than the left. They were pointed in different directions.”

Such paralysis cannot be reversed, so Chu’s remedy was to surgically weaken the muscle opposite the damaged one. This brought Kube’s eyes back into alignment, and put him back in the ring.

Within two weeks he was doing roadwork, and eight weeks after surgery, Punk Kube won the 1987 Golden Gloves Championship in St. Louis. He has since gone on to claim first place in the regional Junior Olympics for his age and weight category.

“Dr. Chu called Punk the night before the Golden Gloves fight to wish him good luck,” says the elder Kube. “That really meant a lot to him.”

The eye care center employs the latest advances in the fast-changing field of pediatric ophthalmology. New surgical microscopes, high-powered surgical lasers and precision suction devices that remove cataracts are in regular use. But when looking to the future, the center’s clinicians take their cues from researchers at the Washington University School of Medicine. One promising area concerns diagnosis.

“A difficult thing about working with children is trying to measure acuity,” says Chu. “You can ask an adult to read an eye chart, describe his vision, . . . but you can’t expect a newborn or young child to articulate what it is they are seeing.” The goal for researchers, according to Chu, is to develop some physiological, objective measure of acuity independent of the patient’s communication skills.

Another great problem of working with children is also one of its greatest advantages—plasticity. “Children’s bodies and brains are still growing, changing, adapting,” Chu says. “For something like amblyopia, or ‘lazy eye,’ this plasticity works in our favor. If we catch the problem early, the mechanical and neurological make-up of the patient is flexible enough to incorporate change. Normal or near-normal sight can be achieved.”

If a lazy eye is left untreated, however, damage in the brain representing that eye becomes permanent. “Even if we surgically realign the eyes of an adult with strabismus, for example, normal vision is not restored,” Chu says. “There may be no damage to the eye itself, but the mechanisms responsible for transmitting and processing visual information are selectively underdeveloped, and the brain loses the capability to employ information from that source. The eye is turned off.”

Plasticity works against pediatric ophthalmologists when stability proves to be ineffective treatment. For example, when a cloudy lens, or cataract, is removed from an adult’s eye, an artificial lens may be implanted in its place. A real lens would change in power as a child grows. But with an implant, a child would still have to use glasses or contact lenses to accommodate a lens that doesn’t grow.

But regardless of the technology and skills offered by the eye care center, it’s the personal attention of Chu and his staff that attracts most patients. “I have three young children of my own,” Chu says. “Every time I treat a patient, I think about my own children and ask myself, ‘Would I do the same for them?’ It makes me think very carefully about every single move I make.”

And in the end, this intangible commodity of understanding may be the single most important element of care at the center. “The best measure of progress is the number of satisfied patients and parents,” Chu says. “We aim to make plenty of both.”
Reflecting upon his six-month stay in St. Louis while visiting Colin Painter, Ph.D., professor of otolaryngology at Washington University School of Medicine’s Speech Science Lab, Sohtaro Komiyama, M.D., assistant professor of otolaryngology at Kyushu University in Fukuoka, Japan, writes: “I believe that people in St. Louis are big-hearted because their country is so big. Their table also reflects the size of their country—there are usually huge quantities of food.

Contemplations about size and population density may make it seem that God has not been fair to us Japanese. However, I think that this kind of thinking is wrong. America seems to be in a state of war—white people against black people, immigrants against American born, rich against poor. . . . To understand the situation in America, it may help to think about war as an example. If you are in enemy territory, to survive, you must know where the safe places are. I believe that many Americans look at their cars and houses as the few safe places in enemy territory. Thinking this way, I began to realize that although Americans live in a very big country, they really feel safe in a very small area.”

Komiyama is one of many Japanese scientists who have, at one time or another, passed through the laboratories at the School of Medicine. These visits from Japan have not only provided a vehicle for fruitful scientific interchange between the United States and Japan, but also have given these Japanese guests the chance to experience Western culture. Observing a different culture is a good opportunity to look at one’s own culture, according to Tetsuo Otani, M.D., a postdoctoral fellow from Kobe University in Kobe, Japan, who is here studying placental hormones with Irving Boime, Ph.D., professor of obstetrics and gynecology, and pharmacology. “If you just live in your own culture, you don’t notice it as much,” he remarks. “You take it for granted.”

Few Americans, on the other hand, have had a similar opportunity to study in a Japanese lab, because the Japanese have had few, if any, formal research exchange programs to support foreign trainees and investigators.

A major step in this direction was made last spring, when nine faculty members from Washington University School of Medicine traveled to Tokyo to inaugurate the first truly reciprocal exchange program between an American university and a Japanese research institute—the Tsukuba Life Science Center of Japan’s preeminent government-sponsored research institution, RIKKEN. Similar to another exchange program RIKKEN established with the Pasteur Institute in Paris last year, the new program with the School of Medicine is designed not only to foster research collaborations, but also to encourage scientists from both institutions to share techniques and teaching skills through joint meetings and exchange visits.

The opening symposium in Tokyo last spring, which featured some of the hottest topics in cell biology and immunology, was one of two inaugural events for the exchange program. Next spring, scientists from RIKKEN will attend a sister symposium in St. Louis. While the fine details of the exchange will not be completely worked out until next spring,
faculty members who attended the meeting in Tokyo have strong hopes that the program may have a ripple effect, encouraging all sorts of collaborative ventures and exchange of young faculty.

Of all the American universities the Japanese could have selected for this exchange, they chose Washington University because of its strong programs in immunology and cell-growth regulation. During the initial planning for this exchange, scientists from RIKKEN visited the School of Medicine’s hybridoma facility, where very specific antibodies are made and stored. Personal contacts and long-standing ties between the two institutions were also important. “In all dealings with the Japanese, they first want to know you as a person—your background, your family, your interests,” David Schlessinger, Ph.D., professor of medicine, and microbiology and immunology, explains. “Then, after they know who you are, they get down to the business at hand.”

Boime experienced this Japanese approach to business when he spent three months last year as a visiting professor at Kobe University. His Japanese hosts quickly learned that Boime, who is an Orthodox Jew, could not eat certain foods. After his first dinner in Japan, all of his hosts had familiarized themselves with these food restrictions and, from then on, served him vegetarian dinners and foods that would not violate kosher laws.

Americans are much more trusting that contracts form the basis for long-term relationships, according to Harvey R. Colten, M.D., Harriet B. Speohr Professor and head of pediatrics, one of the nine faculty members who, along with Schlessinger, attended the symposium in Tokyo. “To the Japanese, a contract is only an affirmation of an already existing relationship.”

Schlessinger’s own friendship with Fumio Imamoto, a microbiologist from RIKKEN who has been heading the international exchange effort, played a role in solidifying the School of Medicine’s relationship with the Japanese. Schlessinger and Imamoto have been friends and colleagues since the 1970s, when they worked together on bacterial gene expression.

Another strong tie with Japan exists in the Department of Otolaryngology, where many Japanese ear, nose and throat specialists trained under the late former department head Joseph H. Ogura, M.D. Approximately 30 of Ogura’s former trainees—many of whom now heads of their own respective departments in Japan—have even formed their own alumni association, which meets on a regular basis.

Most of the faculty members who attended the symposium at RIKKEN have at least one tie with Japanese researchers. Colten, who has been to Japan three times—twice for international immunology conferences and once as a visiting professor at Kanazawa Medical School—is a firm believer that diversity in the lab setting helps to generate truly imaginative solutions to problems. His own laboratory visitors have included a large representation of Japanese.

Colton is a lover of oriental culture, having cultivated Bonsai trees for many years. He has also learned many as 750 Chinese characters, placing him at the fourth-grade reading level (2,000 characters are needed to read the newspaper).

“Learning the characters is not only fun,” he says, “but the combination of characters also tells you something about how oriental people view life. The word steam, for example, is a combination of the characters for water and spirit. Poem is made of the characters for word and temple.”

Although Schlessinger has not yet attempted the written word, he is learning to speak Japanese at night school in Washington University’s University College. “The people in our class represent all ages and types of people from businessmen to literature majors,” he says. “That so many different types of people would want to learn Japanese, I think, indicates how powerful Japan has become, and how much interest there is in Japanese culture.” That, in a nutshell, is what the exchange is all about, Schlessinger explains. “Scientists have always gone to places where there’s good, strong science. They’ve studied in France; they’ve studied in England; they’ve studied in the United States. Why shouldn’t they study in Japan?”

School of Medicine investigators and trainees who visit RIKKEN under the new exchange program (which will most likely start out modestly, with the exchange of only one or two people from each institution) will not only experience a different culture, but also different styles of science and medicine.

In addition to some small laboratories run by relatively independent professors who apply for their own funds, the Japanese more often work in huge laboratories under one main boss, or department head, who controls all of the grant money. Salaries are not paid out of grants, but by the government, according to a fixed rate. The result is that the majority of funds flow to older researchers with more established reputations. For many long-term projects this arrangement is effective, although younger researchers often have the most innovative, if yet untested, ideas.

The Japanese also tend to be very strong in the chemical and physical sciences, and are very adept at transferring basic science and technology to industry, according to Joseph M. Davie, M.D., Ph.D., professor and head of microbiology and immunology, who also attended the RIKKEN symposium. This being the case, School of Medicine researchers should be able to learn a great deal in Japan, according to Boime. “Whenever scientists get together, they always learn something.”

Other faculty members who attended the RIKKEN symposium were: Thomas F. Deuel, M.D., professor of biological chemistry and medicine; Elliot L. Elson, Ph.D., professor of biological chemistry; Eugene M. Johnson Jr., Ph.D., professor of pharmacology; William H. Daughaday, Irene C. and Michael M. Karl Professor of Endocrinology and Metabolism in Medicine; Philip Needleman, Ph.D., Alumni Professor and head of pharmacology; and Carl W. Pierce, M.D., Ph.D., Wilma and Roswell Messing Professor of Pathology and professor of microbiology and immunology.
Imagine a map that changes if you try to look at it. As you cast your attention to it, roadways automatically alter and intersections permute. Consider the uncertainty, the ambiguity, the ponderousness of such a thing.

Scientists trying to map the human brain have faced the frustrations of just such a paradox. Limited by methods of study that were fundamentally invasive, they could never be sure that their methodology hadn't changed or tainted the map. As a result, a detailed, accurate map of functional zones in the normal human brain has been out of science's grasp—until recently.

PET scanning, or Positron Emission Tomography, a technology developed more than a decade ago in the Division of Radiation Sciences at Mallinckrodt Institute of Radiology by Professor M. Michel Ter-Pogossian, Ph.D.,

Tracing the SENSES

BY DON CLAYTON
combined. The device consists of a circuit about the size of standard dice. While a decade of experience in PET, summarizes the tremendous recent gains this way: "Even those of us who know and use PET are excited that we can now get down to the level of mapping discreet functional changes in the brain; that we can localize so precisely both normal and pathological brain functions."

Just two to three years ago, the best PET machines couldn't resolve beyond the 1.5- to 2-centimeter range—a cube about the size of standard dice. While that was and is useful in some studies, to begin to think in real terms of how the brain works, that resolution was coarse, crude.

"However, with the strides made recently, we now have PET localizing areas of function in the 1- to 2-millimeter range. That's improvement to an order of magnitude we wouldn't have predicted a short time ago," Raichle adds.

The PET scanner is, in simple terms, a Geiger counter, camera and computer combined. The device consists of a circular array of radiation-sensing tubes that are activated by packets of energy shed by radioactive particles in much the same way that light exposes film in a camera. Impulses from the individual detection tubes are then combined by a computer into a single image. To undergo a PET scan, the subject is placed in the doughnut-shaped machine and then injected with or inhales molecules that have been labeled with a radioactive tag. These molecules slip into the body's biochemical traffic and congregate preferentially in areas where their biological activity is in demand. The radiation they shed is picked up by the detectors and converted to the electrical impulses that the scanner's computer integrates into an image.

During the late 1970s here at Washington University, a team headed by Raichle helped develop the use of radiolabeled water injected into the bloodstream as a way for PET to map changes in blood flow. Their interest was, in part, based on the fact that as brain cells in an area increase their activity, there is a corresponding increase in blood flow to that area. By 1980, labeled water had become a proven and safe method of detecting relative functional changes in different areas of the brain.

At the same time, several other researchers around the country were working on an alternate molecular tag, labeled glucose, to study brain metabolism in man. But the Washington University group's efforts in brain blood flow with oxygen-labeled water provided a big advantage: the ability to quickly do several scans on a single subject.

The half-life of labeled water is so brief (2 minutes) that it is essentially spent in less than 10 minutes, a very brief period when compared to the hour or so needed for glucose to shed its radioactivity. Allowing several minutes for the radiation to be depleted and return to "base line" between scans, scientists monitoring blood flow changes can do eight scans on a subject in less time than labeled glucose requires for a single scan.

"First we take a resting-state scan, then we apply a stimulus or ask the subject to perform a task and scan again," explains Peter Fox, M.D., an assistant professor of neurology and radiology, who now routinely uses PET scanning to map the human brain. "By comparing resting-state and activation-state images, we can map the brain region involved in a specific function."

While PET imaging with oxygen-labeled water lends itself beautifully to functional brain mapping, it can support a broad range of investigations. Fox and a group of co-workers have focused on activation studies. Eric Reiman, assistant professor of psychiatry, is engaged in applying PET to the study of mental disorders. Joel Perlmutter, M.D., assistant professor of neurology and radiology, joined the team hoping to further develop PET as a tool in studying neurotransmitters, among other things. Their interests, combined with Raichle's, led to a burst of activity in applying and refining PET scanning for human brain studies.

The success of activation studies depends on two things: how precise you are in controlling and presenting the activating stimulus or task, and the ingenuity with which you glean useful information and images out of the mountains of data the studies generate. Fox and collaborators have devised a variety of elegant activation protocols in which a single variable is manipulated to identify the brain regions that mediate these very specific functions.

Two of the brain activation studies that Fox has worked on more recently illustrate the value of presenting the stimulus in a way that is controllable, simple and maximizes the chance of a measurable result. To chart the brain areas that receive tactile information from different parts of the body, he has used a vibration to stimulate small surfaces on the lips, fingers and toes. Brain response to stimulation of each part of the body was intense and focal—tactile stimulation of each different part of the body telegraphed a corresponding increase in metabolism to separate, distinguishable parts of the brain.

The results were consistent in repeated trials in individual subjects, and all eight volunteers tested showed the same response locales.

In another example, Fox, working with Michael Posner, Ph.D., professor of neuropsychology, and Steven Petersen, Ph.D., research assistant professor of neuropsychology, developed a protocol to study which brain areas are recruited for various stages of language formulation. Posner is an expert in the regulation of attention and the nature of cognition.

"Our approach in such a case," Fox says, "was to first examine the current wisdom and determine which brain areas we would expect to be involved in language generation. Then we would look to those areas to see if we could describe, using the PET scanner, what conditions are necessary and sufficient for activating those same areas. We attempted to break down, step-by-step, what we conceive of as incremental levels of function in language. First we would show the subject a
word, then during the next scan ask them to repeat the word out loud. In the third scan, they were not to repeat the word they were shown, but rather to say a related word. That caused them to make a semantic association. As we go through these stages in the language process, we can determine which areas of the brain are activated by these levels of function and which are not.

It wasn't always so easy to analyze the data in a way that permitted useful comparisons between resting (normal) and task-driven images. The precise protocols for applying stimuli and the general knowledge of where to look for responses only solved the first part of the enigma. The second part—how to extract useful information from the huge amount of data—was equally crucial to the PET boom.

"We've been doing activation studies here for six or seven years, a long time," says Fox. "At that earliest stage, image analysis or data analysis at the level now routine hadn't even been conceived."

Raichle and Peter Hirschovitch, M.D., an early member of the PET team who now conducts PET research at NIH, had designed as early as 1980 an activation study to map the processing of simple sounds. The images were so cluttered with noise that no clear signals attributable to sound-processing were apparent.

"They ran into the problem of not knowing how to analyze the data in a way that could detect and ferret out the response," Fox explains. "They went on for a while trying to change the stimulus, but they knew the problem was in handling the data, so they abandoned the protocol to pursue more fruitful research."

Fox was soon in a position to empathize with those who had tried activation studies before him. After only his first few months of using the PET scanner, he ran into the same trouble. "Like them," he adds, "I just couldn't authenticate a response."

At that point, Fox approached Mark Mintun, M.D., then a resident, now assistant professor of nuclear medicine, for help. As a third-year medical student, Mintun had written the computer programs used to generate the images that were state-of-the-art at that time. Those programs converted the data into images that revealed broad regional differences in metabolism, such as an imbalance between the left and right sides of the brain, but could not improve the signal-to-noise ratio enough to usefully image the slight metabolic fluctuations created in the early activation studies.

"I asked Mark to help me manipulate and analyze the images," recalls Fox. "That was about five years ago, and Mark and I are still talking, everyday, about how to manipulate images."

Mintun, who describes himself as a person who simply likes to "show others new ways of looking at their data," was diligent and optimistic in his work in PET scan data analysis and has now developed a variety of techniques that, more than any other contributions, have made possible the recent manifold improvements in PET's resolving power.

The first shot in the salvo of software was a program that enabled Fox, Perlmutter and all the PET users to take a pair of images, one from a resting state and the other from an activated state, for example, and lay one over the other mathematically and subtract it. This function created an entirely new image of the absolute differences between the two original scans.

"And then, Bingo! Things really started happening," comments Fox. "At that same time, I switched from tactile to visual stimulation of normal subjects for technical reasons and was getting great, robust, intensely focal responses. The ability to subtract away the part of the image that corresponded to the control, or resting state, tore down the barriers."

Image subtraction not only improved localization, it also improved sensitivity by removing subjective bias from the assignment of "hot", or activated, areas of the brain. No longer did researchers have to pin up the before and after images side-by-side and guess which areas were showing significant change and which were not. The chances that significant change would be judged insignificant, or vice-versa, were greatly reduced.
Several additional advances even further refined image subtraction’s ability to localize responses. Mintun developed a program that automatically lined up corresponding landmarks in the images. There was a reduction in the fuzzy borders of some activation sites by electronically nullifying the artifacts due to patient movement.

According to Mintun, who is now on the full-time faculty in nuclear medicine, an even more important contribution was a series of program changes that enabled them to study very subtle responses in the brain, the kind of changes that can’t always be seen in every individual, or in every scan of any one individual. “The logical thing, we thought, would be to add up and then average the responses from patient to patient,” he says. “We knew it wouldn’t tell us anything about one scan or one subject, but it would tell us something of scientific interest regarding the general principles of brain function. So, we developed techniques to turn every individual brain scan into a standard format equal in shape, size and orientation. When combined and mapped into the standard format, suddenly hard-to-see responses in individuals became obvious on the aggregate image.”

These data analysis tools have propelled PET scanning to new promise. “There’s no end in sight to what we can do,” claims Fox. “I have no doubt that, in addition to our progress in mapping functional zones in the normal human brain, PET scanning will be employed on many different levels, even including the clinical setting.”

Mintun and nuclear medicine chief Barry Siegel are now installing a scanner in the recently renovated space of the nuclear medicine division, anticipating that soon clinicians will want to employ the power of PET in evaluating brain function in their patients.

“Mapping functional parts of the brain prior to neurosurgery should be very straightforward and may be useful clinically,” says Mintun. Activation studies that reveal the precise location of a particular person’s language center, or the location for control of the hands, for example, may be useful as a guide for a neurosurgeon who must remove a tumor or focal area of epilepsy but wants to minimize damage to other crucial areas.

Because the techniques enable clinicians to realign and subtract images taken months, even years apart, psychiatrists may soon use PET to monitor the effects of psychoactive medications by comparing a premedication scan to scans taken at intervals during the course of therapy. Reiman and Raichle, who have backlogged scans of patients with panic attack as well as schizophrenia can soon subtract scans of normal volunteers from scans of their patients in the hope of elucidating or mapping the biochemical imbalances that cause these disorders.

“We have done so many normal scans,” explains Mintun, “that we have a sound base of knowledge about which types of tasks turn on certain areas of the brain. Peter Fox has gorgeous protocols in language, cognition, vision, hearing and tactile sensations which clearly show that for each specific task, one area of the brain turns on another that turns on another.

What we would like to do is to take people who we know have an abnormality in how they think or in their ability to understand the world, and find out at what point the abnormality manifests itself. In schizophrenia, for instance, is the abnormality out in the primary areas of the brain or is it in the more complicated, associative areas? That type of work may not have much immediate clinical relevance, but the concept of being able to understand where the breakdown in communication is in these illnesses is—exciting, there’s no other word for it.”
The percentage of seniors who matched with one of their top three residency choices is higher this year than it was last year, according to Elmer B. Brown Jr., M.D., associate dean for continuing medical education and postgraduate education. Eighty-six percent of the Washington University students who participated in the National Match ended up with one of their top three choices, while 63 percent matched with their first choice, he reports.

One-hundred-and-one seniors from a class of 118 participated in the match, while 17 students—most of them M.D./Ph.D. candidates—placed into research or other programs outside the match. Of those who participated in the match, three failed to match initially, but found positions by the end of the day.

As a result of the match, 36 percent of this year's graduating class will remain in St. Louis—half of whom will train at Barnes Hospital. The remaining 64 percent will train in 29 other states.

Internal medicine and surgery drew a smaller proportion of students this year, while pathology, family practice and radiology claimed more seniors than last year.

Approximately 39 percent of the first-year residency appointments were in internal medicine, 14 percent in pediatrics, 9 percent in surgery, 6 percent in pathology, 6 percent in psychiatry, 6 percent in family practice, 4 percent in obstetrics and gynecology, 3 percent in radiology, 3 percent in emergency medicine and 1 percent each in orthopedic surgery, urology and otolaryngology. An additional 4 percent were placed into rotating, flex or transitional programs, while the remaining 3 percent are not taking a residency.

The class of 1987 and their first-year appointments are as follows:

**Alabama**

Birmingham
University of Alabama Hospitals
Wayne Giles, Internal Medicine

**Arizona**

Tucson
Tucson Hospital Medical Center
Debra Friedman, Transitional Medicine
Gregory Pennock, Internal Medicine
Linda Stevenson, Emergency Medicine

(Left to right) Gary Gretch, Tim Pluard, Jesse Little, Grant Rogero and Brent Layton scramble for their matches.
Patrick Sandiford (left), Philip Lee (center) and Norm Schmidt share the good news of their first-year residency appointments.

California

French Camp
San Joaquin General Hospital
Norman Schmidt, Family Practice

Fresno
Valley Medical Center
Anne Palma, Internal Medicine
Grant Rogero, Internal Medicine Preliminary

Los Angeles
Children's Hospital
Craig MacArthur, Pediatrics
UCLA Medical Center
William Aronson, Urology
David Jick, Internal Medicine

Oakland
Highland General Hospital
Robert Burri, Transitional

San Diego
University of California
Scott Zager, Internal Medicine

San Francisco
University of California
William Plautz, Family Practice

San Pedro
San Pedro Peninsula Hospital
Steven Curran, Family Practice

Sepulvada
UCLA/San Fernando Valley/VA Medical Center
Justin Starren, Internal Medicine Preliminary

Stanford
Stanford University Hospital
Charles Baurn, Pathology
Philip Lee, Internal Medicine

Torrance
Harbor-UCLA Medical Center
Pejman Salimpour, Pediatrics Primary

Colorado

Denver
University of Colorado School of Medicine
Roderic Smith, Pediatrics

Connecticut

New Haven
Yale-New Haven Hospital
Paul Martin, Pediatrics

Florida

Miami
Mt. Sinai Medical Center
Carlos Buznego, Internal Medicine Preliminary

Georgia

Atlanta
Emory University School of Medicine
Keith Churchwell, Internal Medicine

Hawaii

Honolulu
Tripler Army Medical Center
Christopher Meyer, Internal Medicine

Illinois

Chicago
Children's Memorial Hospital
William MacKendrick, Pediatrics
Sarah Mahaffy, Pediatrics
Illinois Masonic Medical Center
Eugene Cabianelli, Transitional
A friend looks on as Tim Pluard discovers where he will go for his first-year residency. One-hundred-and-one seniors from the School of Medicine participated in this year's match. Eighty-six percent ended up with one of their top three choices.
Steve Cragle (right) looks on as Dirk Baumann reads his match. Baumann will serve his first-year surgical residency at Barnes Hospital next year. Nine percent of this year's class received first-year appointments in surgery.

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The intense, searing light of the laser has evolved into a remarkable medical instrument. It has revolutionized some procedures in ophthalmology, plastic surgery, gynecology and neurosurgery; it holds great promise for the diagnosis and treatment of a variety of human illnesses. Yet many specialists express a growing concern, not about the technology itself, but about its marketing and promotion.

The public's captivation with laser technology—a fascination that began when the laser beam was first harnessed in the laboratory in 1969—is well-founded. Surgical lasers cut through tissue with extreme precision. They cauterize blood vessels as they cut, minimizing bleeding. They virtually eliminate the chance of infection that exists with conventional instruments. They are fast and in some cases painless.

Yet precisely because the laser's bright light has captured the public imagination, its lure as a marketing tool has increased. The potential exists today for overuse or misuse by doctors eager to take advantage of its appeal as an instrument of public relations as well as medicine.

Until recently, only hospitals and medical centers could afford surgical lasers, where they are monitored by peer review and credentialing boards. Major hospitals have established laser committees to certify that doctors using the equipment are properly trained and that the procedures they use are accepted as beneficial and appropriate.

But recently developed, inexpensive lasers—costing as little as $20,000—may soon become commonplace in outpatient clinics, ambulatory care centers and doc-
... the general public needs to be critically aware that medical procedures are not necessarily safer or better simply because they are performed with a laser.

tors' offices. In these settings, appropriateness of use becomes a fundamental issue.

The dermatologist who advertises that he or she will use a laser to remove a simple wart from the hand or foot may not explain to patients that the wart can be removed at least as effectively by less expensive and more conventional means—the $3 disposable scalpel, for example.

The public is already being swayed by advertisements touting "laser facelifts." Yet in this procedure, the laser simply makes an incision. There is no medical evidence to suggest that it performs the task better than the old-fashioned surgical blade.

Another recent application of the technology is laser circumcision. While the laser is certainly capable of performing the procedure, conventional methods are at least as good, perhaps better and almost certainly less expensive. Without question, lasers perform important functions in many medical fields. Numerous new applications are being examined, and some of these will eventually prove effective as our knowledge of the technology advances.

But there is a tendency to overstate the use of lasers. Some doctors, for example, have advertised "laser cataract surgery," encouraging patients to believe that lasers have replaced conventional procedures. The laser does, in fact, play an important role in cataract surgery, but only after the clouded lens has already been cut away using conventional methods.

By promoting these types of marginal laser techniques, institutions tell the public: "We use lasers—the most advanced care. Come here for treatment." A patient then visits the family physician and asks, "Can you give me laser treatment?" If the doctor says "no," he stands to lose the patient.

Some have suggested that a national review board certify physicians in laser medicine through a nationally administered credentialing procedure. Are we to establish such boards for every new piece of technology developed? Each new application? Certainly such a task will be costly, cumbersome, difficult to effectively administer and, in the end, unnecessary.

Society has bestowed upon physicians a high degree of autonomy through a social contract of mutual trust. The review and accrediting procedures now in place in the nation's medical schools, hospitals and medical societies have in general served the public well. And, in most cases, we can continue to rely on these checks and balances to insure that medical professionals using these instruments are trained properly.

We cannot point a finger at any one person or group. Certainly, the overwhelming majority of physicians use lasers wisely and effectively. But the general public needs to be critically aware that medical procedures are not necessarily safer or better simply because they are performed with a laser.

Ultimately, responsibility for appropriate use of lasers rests, as in other areas of medicine, in the mutual trust between patient and physician. Before submitting to laser surgery, patients should be sure the doctor is board-certified in his or her specialty, a member of local and national medical societies, on a reputable hospital staff and has experience and training with laser procedures. When there is doubt, get a second opinion.

The use of lasers should and will continue to expand rapidly. Even those who use the laser daily, marvel at its ability. But both physician and patient must acknowledge that, like other medical tools, the laser is nothing more than an instrument. True, it's on the cutting edge of technology, but must be used only when it is the most appropriate and effective tool available.

George M. Bohigian, M.D., is associate clinical professor of ophthalmology at Washington University School of Medicine and chairman of the Panel on Lasers in Surgery and Medicine of the American Medical Association's Council on Scientific Affairs.
Robert and Nancy Kolodny
hadn’t planned on writing a book for kids
when they wrote *How to Survive
Your Adolescent’s Adolescence*. Their
second co-authored book, *Smart Choices*,

Robert and Nancy Kolodny have three adolescent-age daughters of their own: Lisa (top), Linda (left) and Lora (right).
one of three books this year to be named “best books for teenagers” by the New York Public Library system, was written upon the request of the teenagers themselves. “We received letters from kids whose parents had read our first book that asked, ‘Why just write a book for parents? We need a book too,’” Nancy says.

Together, the two books serve as a vehicle for family discussion, according to the husband and wife co-authors, who are both Washington University alumni. “Most problems encountered by teenagers and their parents boil down to this communications aspect,” Nancy explains. “No one can avoid all problems. But if that communication is there, normal, everyday problems generally won’t turn into major crises or life-threatening problems.”

Communication with their own teenage daughters, in fact, added substantially to the impact of Smart Choices. The Kolodnys’ two oldest daughters, Linda and Lora, not only served as critics for the book, but also suggested some of the anecdotes. Yet while many of the strategies suggested in the books have actually worked very well in his own family, Robert emphasizes that the books serve a much larger purpose than “Gee, this is the recipe I use at home.”

Before writing the books, the Kolodnys analyzed hundreds of interviews with parents and kids from all over the country, pinpointing problems people have, as well as the things that keep them from resolving those problems. In doing so, they drew from experiences and insights gained in their respective fields of psychiatry and social work.

A 1969 graduate of the School of Medicine, Robert brought to the books more than a decade of Masters and Johnson Institute research on pubertal development and use of illicit drugs. Nancy, who graduated from Washington University in 1969 with a master’s degree in English, and again in 1980 with a master’s in social work, contributed her knowledge and counseling experiences in the area of eating disorders.

The Kolodnys began How to Survive Your Adolescent’s Adolescence in 1982, after they’d already done so much editing of each other’s projects that they finally said, “Why not do something together?” Robert had previously done a great deal of writing for journals during his years at Masters and Johnson, but admits that How to Survive Your Adolescent’s Adolescence required that he first “unlearn some of the bad habits of medical writing.”

How to Survive Your Adolescent’s Adolescence emphasizes positive parenting, an approach that promotes nurturing, growth-enhancing parental attitudes and behaviors; preventive strategies that can help teens avoid major problems in their lives; and crisis-solving skills for dealing effectively with disasters when they occur.

It is a cornucopia of practical information on anything parents ever wanted to know about teenagers, but were afraid to ask. And, in light of this information, it provides parents with specific strategies they can use to help their teens get through some rough years. In the chapters on drugs, for example, parents are given a checklist of dos and don’ts for talking to their kids about drugs that include being open and direct, avoiding scare tactics, giving teens ammunition for recognizing and dealing with peer pressure, setting clear limits and explaining what will happen if those limits are ignored, and letting teens know that their parents are available when needed.

For occasions when these strategies don’t work, the Kolodnys provide parents with information that will help them differentiate major crises from everyday problems. In the chapter, “A Parents Primer on Teenage Alcohol and Drug Abuse,” they include a detection list of 18 signs and symptoms.

Most important of all, How to Survive Your Adolescent’s Adolescence advises parents what to do and how to find professional help during a crisis. In the drug chapters, for instance, the Kolodnys list 11 steps parents can take if they discover their teen is abusing drugs or alcohol. The book provides similar problem-solving strategies for sexual matters, academics, self esteem, social skills and anti-social behavior, as well as covering issues of divorce, teenage pregnancy, runaways, cults, suicide, and when to call in a professional or the police.

Complementary information for teenagers is contained in Smart Choices. Of special interest to teens with professional or successful parents is the section, “Is it OK to Be Average?” The Kolodnys answer with an emphatic yes, “Physicians and other professionals tend, as a group, to have exceptionally high expectations for their kids in terms of educational and occupational goals, and may be very upset with a kid who has a B minus average,” Robert says. “They can better understand this kind of thinking if they liken themselves to the parent who used to be a football star and tries to push his kid to be a star,” he explains. “When we expect our kids to be automatically academically excellent, that’s a heavy load for them to bear.”

Smart Choices does not talk down to or preach at teens, but draws heavily from the experiences of the “real experts”—teenagers who spoke with the Kolodnys and gave them suggestions based on their own experiences. Smart Choices was, after all, written to help teenagers make smart choices. As the Kolodnys explain in their introduction, “We hope our book can help you turn yourself into a winner.”

Two other co-authors contributed to How to Survive Your Adolescent’s Adolescence: Thomas E. Bratcher and Cheryl Deep; the former also contributed to Smart Choices.
From East Coast to West Coast: Alfred M. Markowitz, M.D. ’52, and his wife, Sydell (front) and Amos H. Lieberman, M.D. ’52, and his wife Elaine (rear) ride the train through the St. Louis Zoo. Classmates and friends, Markowitz (from New York) and Lieberman (from San Francisco) enjoyed visiting together on their 35th class reunion.

Members of the Class of 1962 and their wives pore over photos at the reunion dinner dance.
Dana C. Ryan Jr., M.D. '52 (left) goes over the tour schedule with a shuttle bus driver. The Medical Center Alumni Association sponsored trips to several sights, among them the Missouri Botanical Gardens, the St. Louis Zoo, Union Station, the Anheuser-Busch Brewery and the riverfront.

Gilbert Goldman, M.D. '37, and his wife, Elise, step out at the reunion dance.
Edward Harris, M.D. '37 (left) and Martin Compton, M.D. '37, reminisce during their Friday evening class dinner.

Fashion design students from the Hilltop campus entertain wives with a fashion show.

Senior medical students (left to right) Bob Tolan, Jeff Feldman, Keith Churchwell and Steve Cragle entertain alumni during the Saturday evening reunion dinner dance.
Alumni and Faculty Awards

Alumni/Faculty Award recipient Stuart Kornfeld, M.D. '62, cuts the rug at the reunion dance. Alumni/Faculty Awards were also given to Sidney Goldring, M.D. '47, Virgil Loeb Jr., M.D. '44, and Gerald Medoff, M.D. '62. Alumni Achievement Awards were given to Pedro Cuatrecasas, M.D. '62, Alfred Gelhorn, M.D. '37, and C. Barber Mueller, M.D. '42. For more information about the award recipients, contact the Medical Center Alumni Association, Box 8049, 660 S. Euclid, St. Louis, MO 63110.

The family dog, Lacey, looks on as Robert Fry, M.D. '72, and his wife, Susan, entertain members of his class at their home in the Central West End.
Harold R. Lyddon, M.D. '37, and his wife, Marion, enjoy the orchids during a reunion weekend shuttle bus tour of the Missouri Botanical Gardens.
This spring, the School of Medicine graduated 118 M.D. candidates, 18 occupational therapists, 21 health administrators and 2 physical therapists.