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David Kessler, JD, MD, commissioner of the U.S. Food and Drug Administration, congratulates Andrew Greenlund, left, and Howard Rogers, who received their MD/PhD degrees on May 17. Kessler was the guest speaker at the School of Medicine commencement ceremony on the Hilltop Campus. The title of Kessler's address was "Doctors and Healers."
The photo illustration shows a sonogram of a 12-week-old fetus against the graphic tracings of an electrocardiogram (EKG). To learn more about how the work of a School of Medicine cardiologist is guiding women with serious cardiac conditions through pregnancy, turn to page 12. Computer illustration by Amy Zinsmeyer.

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Doing Good Deeds

CAROL S. North, MD

When the floodwaters receded, the program was expanded to include crisis services for situations such as violence in schools and elder abuse. In her position as chairperson of the Disaster Committee for the Eastern Missouri Psychiatric Society, North developed a program for area psychiatrists to provide free services at area hospitals.

Hats Off To Raichle

MARCUS E. Raichle, MD, professor of radiology, is one of 60 new members elected into the prestigious National Academy of Sciences. Election into the organization is considered one of the highest honors that can be accorded a scientist in the United States.

Raichle, who is co-director of the division of radiation sciences at Washington University’s Mallinckrodt Institute of Radiology, also is a professor of neurology and a senior fellow with the university’s McDonnell Center for Studies of Higher Brain Function.

He is known for his pioneering research in the use of positron emission tomography (PET) to map specific brain areas at work in tasks such as seeing, hearing and speaking. PET allows researchers to noninvasively study the living human brain and to track and record its function.

Raichle’s research has helped in the development of a brain atlas that specifically maps brain regions responsible for language and thought processing. By using PET to measure bloodflow and metabolism, Raichle and fellow investigators have shown how the brain responds when a subject is asked to memorize words or to think sad thoughts. In addition, they have mapped areas involved in attention, analyzed chemical receptors in the brain, investigated the origin and physiology of seizure disorders and evaluated patients at risk for stroke.

The National Academy of Sciences is a private organization dedicated to furthering science and its use for the general welfare.

NAS Council Taps Kipnis

DAVID M. Kipnis, MD, Distinguished University Professor of Medicine and professor of molecular biology and pharmacology, has been elected to a three-year term on the Council of the National Academy of Sciences.

Kipnis, who was elected to the National Academy of Sciences in 1984, is internationally renowned as a pioneer in diabetes research. His work has been cited for many honors, including the Endocrine Society’s Ernest Oppenheimer Award and the American Diabetes Association’s Lilly Award and Banting Medal.

Kipnis was head of the Department of Internal Medicine from 1973 to 1992. During that time, the department became
recognized nationally and internationally as one of the foremost academic centers for research and clinical training. Kipnis now devotes most of his time to research as well as work with foundations and corporations. Additionally, he is the chairman of the Scholar Advisory Committee of the Lucille P. Markey Charitable Trust and a member of the board of the Burroughs-Wellcome Trust.

HHS Secretary Names Choi

DENNIS W. Choi, MD, PhD, Andrew B. and Gretchen P. Jones Professor and head of the Department of Neurology, has been named to the National Advisory Neurological Disorders and Stroke Council of the National Institute of Neurological Disorders and Stroke.

Choi was among five physicians, scientists and lay representatives appointed to the council by Donna Shalala, U.S. Secretary of Health and Human Services. The council meets three times a year to review applications from scientists seeking financial support for biomedical research and research training on disorders of the brain and nervous system. The body also advises the institute on research program planning and priorities.

New Appointees Announced

FOUR new appointments recently were announced at the School of Medicine.

Daniel P. Schuster, MD, has been named associate dean for clinical studies; Will R. Ross, MD, has been named associate dean and director of the Office of Diversity; Joan M. Podleski has been appointed assistant dean for clinical operations; and S. Bruce Dowton, MD, (Syd.), has been named associate vice chancellor for medical education.

Schuster is professor of medicine and radiology. In addition to his position as associate dean for clinical studies, he will serve as director of the new Center for Clinical Studies. His responsibilities will include developing the center and establishing an infrastructure for the oversight of industry-sponsored clinical trials of new pharmaceuticals and devices.

Ross, a 1984 graduate of the School of Medicine, comes to the medical school from St. Louis Regional Medical Center, where as vice president for medical affairs, he coordinated the activities of the medical staff, including residents.

In his new position, Ross will lead minority medical student admissions and minority student affairs and also focus on broader issues of diversity. In addition, he will hold the position of assistant professor of medicine, with an appointment in the renal division, where he will continue to see patients and teach.

Podleski formerly was business manager in neurological surgery. In her new role, she will help coordinate School of Medicine clinical operations. She is involved in analysis and planning regarding the possible reorganization of clinical services in a new ambulatory care facility and the creation of an integrated professional practice plan.

Dowton is associate dean for medical education and director of the division of medical genetics in the Department of Pediatrics.

His additional title of associate vice chancellor for medical education reflects the extensive degree to which Dowton manages and coordinates affairs between the School of Medicine and external organizations related to education and training.

Jakschik Awardee

LORA Virginia Hooper, PhD

ORA Virginia Hooper, who recently was awarded a doctor of philosophy in molecular cell biology and biochemistry at the School of Medicine, has received the 1996 Barbara A. Jakschik Award.

The award is presented annually to an outstanding female graduate student in her final year of doctoral research whose thesis focuses on the general area of metabolic regulation. Hooper's dissertation abstract was titled "Purification, Cloning and Characterization of an Oligosaccharide-Specific Sulfotransferase." She completed her thesis work in the laboratory of Jacques U. Baenziger, MD, PhD, professor of pathology and of cell biology and physiology.

Hooper received a cash award, a certificate, and her name was added to a plaque that is permanently displayed in the offices of the Division of Biology and Biomedical Sciences.

The award honors Jakschik, who retired from the Department of Molecular Biology and Pharmacology in 1992 following a career devoted to research on mediators of inflammation.
School Of Medicine Home Page Debuts

The redesigned School of Medicine home page appeared on the WWW in February.

The School of Medicine debuted its revamped home page on the World Wide Web on Feb. 14. The web allows individuals and organizations to post information on home pages. By pointing and clicking on highlighted text, users may move quickly to other pages of interest. The School of Medicine home page provides access to information about news and events, admissions, education and curriculum, research, departments, facilities and services. It is updated regularly. Readers can visit the site at http://medschool.wustl.edu/.

The School of Medicine web site is one of many being created within the institutions of the Medical Center. Others include the home page on the Cochlear Fluids Research Laboratory, developed by Alec N. Salt, PhD, associate professor in otolaryngology. The colorful site offers a pictorial guide to the cochlear fluids as well as an overview of research programs in the department, information on Meniere's disease and an index of ear-related web sites. His pages can be seen at http://lab9924.wustl.edu/.

Alan Pestronk, MD, professor of neurology and pathology, has created web pages on which physicians can list their patients' symptoms, and let the computer program help them decide which disorder best fits the symptoms. His pages can be found at http://neuromuscular.wustl.edu/.

Kathy Mann Koepeke, PhD, executive director of the Alzheimer's Disease Research Center, manages ALZHEIMER. The electronic service gives caregivers access to physicians, researchers and other caregivers. ALZHEIMER's address is http://www.biostat.wustl.edu/alzheimer.

Interesting or informative web sites that were developed at the medical school can receive attention by sending an e-mail message to: kcarlson@ibc.wustl.edu. Outlook will continue to publish web site locations as they are made known.

GenLink Home Page Gets The Point

The Point rating group has ranked the GenLink home page in the top 5 percent of the web.

The GenLink home page has been included in the top 5 percent of sites on the web by the Point rating group. The site was designed by Helen Denis-Keller, PhD, head of the division of human molecular genetics, and her research staff, including Cindy Helms and Li Liu.

The designation entitles the GenLink home page to be listed in the "Top 5 percent of the Web" catalog with other outstanding sites selected by Point editors, who rate and review the most attractive, clever and amusing home pages on the World Wide Web.

Selected sites can display Point's "Top 5 percent of the Web" badge, which lets browsers know the site is worth a stop to look around. Point is a free commercial service and was the first to offer a ratings system.

Visit the site at http://genlink@hdklab.wustl.edu.
Designed With Patients In Mind

The Department of Orthopaedic Surgery has a new home on the 11th floor of Barnes-Jewish Hospital's West Pavilion. The clinic and suite of offices combine former offices from what were Barnes and Jewish hospitals, and incorporate two clinics previously situated in Barnes, and are easily accessible for patients.

The new clinic and business office comprise 14,500 square feet, and house 16 treatment rooms and 16 physician offices. Other conveniences include the large x-ray facility (Mallinckrodt Institute of Radiology) on the 10th floor, which greatly improves patient flow for those awaiting x-rays, and a satellite office of Barnes-Jewish Rehabilitation, which serves patients referred for rehabilitative services.

The Clinical Sciences Research Building remains the hub for orthopaedic research, with the pediatric branch of the department located at St. Louis Children's Hospital. Clinical operations will continue at the North campus (Jewish Hospital's Waldheim Building).

A key element of the restructured department is the development of its research laboratory. The research program will have two foci: repair (including bone, autogenous bone graft, ligament and tendon repair) and adult reconstructive surgery.

Five new clinical faculty have been recruited: Ken Yamaguchi, MD, a specialist in shoulder surgery; K. Daniel Riew, MD, a cervical spine specialist; William J. Maloney, MD, a specialist in adult reconstructive surgery and arthritis surgery; George S. Bassett, MD, a pediatric orthopaedic surgeon; and Joseph Borrelli Jr., MD, who works in adult traumatology.

"An Outpouring Of Emotion"

To express their esteem for a couple who touched the lives of so many physicians, former neurosurgery residents have endowed the Henry G. and Edith R. Schwartz Chair in Neurological Surgery.

Fifty former residents donated a total of $1 million to endow the chair honoring Henry Gerald Schwartz, MD, August A. Busch Jr. Professor Emeritus and Lecturer in Neurological Surgery, and his late wife, Edith R. Schwartz. "This was an outpouring of emotion," says 1963 resident Kenneth R. Smith Jr., MD, now professor and director of the revision of neurosurgery at St. Louis University School of Medicine and president of the Society of Neurological Surgeons.

"The Schwartzes have done so much for us and others. They inspired all who went through the program to become great neurosurgeons and great parents."

Schwartz was head of neurological surgery from 1946 to 1974; he became August A. Busch Jr. Professor in 1970 and took emeritus status in 1984. The program he organized attracted the finest talent in the nation. Out of the 37 residents he fully trained, 16 went on to direct training programs at other U.S. medical schools. Seven of those have been elected president of the Society of Neurological Surgeons, the leading organization for academic neurosurgeons in North America. Five others are full professors in teaching programs.

At age 87, Schwartz remains active in the daily life of the department. He attends conferences, keeps up with the scientific literature and participates in many professional organizations. His wife, "Reedie," whose professional name was Edith Courtenay Robinson, MD, died in December 1994.

Richard H. Schwartz, MD, right, with his father Henry G. Schwartz, MD, reads a letter from a former resident who trained under the elder Schwartz, on the occasion of the establishment of the Henry G. and Edith R. Schwartz Chair in Neurological Surgery.

Outlook Seeks Input From Readers

In the fall issue of Outlook magazine, which will be mailed in October, readers will be asked to participate in a readership survey being conducted by the publications division of the Office of Medical Public Affairs.

A questionnaire will be included in the magazine, with a stamped, self-addressed envelope for convenience. Readers will be asked to critique the fall 1996 issue of Outlook as well as to rate the magazine overall according to appearance, quality and content.

In the 31 years Outlook has been in existence, the magazine has undergone many changes, evolving to its present format. As the quarterly periodical of the School of Medicine, the magazine is one of the primary sources of communication with some 27,500 alumni and friends around the world. The editorial staff is eager to know its readers' thoughts.
Hormones By Design

Irving Boime, PhD

A WASHINGTON University researcher has gone back to the drawing board to make infertility treatments easier on women. By tinkering with reproductive hormones, he is creating forms that may stimulate ovulation without the discomfort of frequent injections or the risk of multiple births.

"Women who take hormones prior to in vitro fertilization or for other infertility problems receive several injections daily," says Irving Boime, PhD, professor of molecular biology and pharmacology and of obstetrics and gynecology. "But we have designed longer-acting versions that might be effective with fewer injections."

Fifteen percent of American couples are infertile. Many of the women who seek treatment receive a pituitary hormone called follicle-stimulating hormone (FSH). Circulating in the bloodstream, FSH binds to cells in the ovary, stimulating egg production. But it can only be given by injections, which must be repeated, because the hormone is broken down after it has circulated.

FSH belongs to a family of hormones called gonadotropins. Each member is made of two related proteins that snap together like building blocks. One protein, the alpha subunit, is the same in all gonadotropins; the beta subunit differs.

Boime took advantage of this difference to improve the FSH molecule. Through genetic manipulation, he created cell lines that secrete a hybrid FSH. The beta subunit of the altered hormone carries a piece of the beta subunit from a related placental hormone. Human chorionic gonadotropin (hCG) maintains pregnancy, and its beta subunit allows it to stay in the bloodstream longer than FSH.

A colleague at Stanford University, Aaron J.W. Hsueh, PhD, found that the new version of FSH survived in animals three times longer than natural FSH.

The modified FSH has been patented, and Organon, a pharmaceutical company in the Netherlands, has licensed the technology for commercial development.

Making The Connection

JOSHUA R. Sanes, PhD, professor of anatomy and neurobiology at the School of Medicine, has received a five-year $4.1 million program grant from the National Institute of Neurological Disorders and Stroke at the National Institutes of Health.

The funds will allow Sanes and collaborators to determine how nerve cells form and disband their connections with other nerve cells or muscle. The research should provide insights into disorders of nervous system development and may suggest ways to encourage injured nerves to regrow.

"These connections are key structures in the nervous system," Sanes says. "As well as linking nerve to muscle, they route information through the brain and play important roles in learning."

Such connections, called synapses, are intricate microscopic structures that involve nerve terminals, muscle membrane and interconnecting components. By altering genes in mice, the collaborators will tease out the roles of the various constituents and the factors that guide synapse development.

Four collaborators will take part in the program. Sanes will focus on a synaptic structure called the basal lamina, exploring its role in synapse development and regeneration.

Jeffery W. Lichtman, MD, PhD, professor of anatomy and neurobiology, will determine how molecules from muscle affect the presence and behavior of nerve terminals.

William D. Snider, MD, PhD, associate professor of neurology, will determine whether a nerve growth factor called neurotrophin-3 guides the axons of developing sensory nerve toward muscle.

Medha Gautam, PhD, research assistant professor in molecular biology and pharmacology, will explore the functions of various proteins in the formation, maturation and maintenance of the neuromuscular synapse.

Obvious Appeal

A PATENT dispute over School of Medicine research has removed a major roadblock for the biotechnology industry.

Thomas F. Deuel, MD, formerly Lewis T. and Rosalind B. Apple Professor of Oncology in Medicine, tried to patent a gene for a protein whose amino acid sequence was partly known. The Patent and Trademark Office (PTO) rejected his application in 1991. But the U.S. Court of Appeals for the Federal Circuit disagreed with the PTO rejection, and told the PTO to resume patent examination.

In the 1980s, Deuel and three colleagues discovered a protein which has the potential to speed wound healing. In 1990, they
applied to patent the protein and DNA sequences encoding the family of heparin-binding proteins. It is the sequence claims that were at the core of the PTO rejection.

Applicants must show that a discovery is useful, novel and not obvious from previously published work. The PTO argued that Deuel’s DNA sequences were obvious because part of the amino acid sequence of related brain proteins had been published.

One hundred and sixty eight amino acids are strung together in a heparin-binding protein, and the sequence of the first 19 was known from the brain proteins. The PTO argued that the ready availability of DNA cloning methods would allow any researcher to determine the DNA sequence of heparin-binding protein using this partial protein sequence. The PTO Board of Patent Appeals and Interferences upheld the decision in November 1993, stating that placing a protein sequence in the public domain also places the sequence of that protein’s gene in the public domain.

In 1994, patent attorneys with Senneger, Powers, Leavitt & Roedel, a St. Louis law firm, filed a brief with the U.S. Court of Appeals on behalf of the then-Jewish Hospital of St. Louis, where Deuel was head of hematology. G. Harley Blosser, principal author of the brief, argued that “what cannot be contemplated or conceived cannot be obvious.”

The court ruled that the DNA sequence that encodes a protein whose amino acid sequence is wholly or partly known is not obvious and therefore can be patented. It considered the obviousness of the DNA sequence itself instead of the obviousness of the method for making such a sequence.

The generalization of this opinion to other patent applications would boost the fortunes of the biotechnology industry, which needs sequence patents to offset some of its business risk.

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**$24 Million Grant To Genome Project**

The School of Medicine is one of six recipients of major grants from the National Center for Human Genome Research (NCHGR) at the National Institutes of Health.

The three-year, $24 million award will allow the school’s Genome Sequencing Center to systematically sequence parts of the human genome to uncover genes and other structures.

The St. Louis group already has sequenced more than 1 million base pairs of human DNA, including the region of chromosome 13 that contains the breast cancer gene BRCA2. The group decided to tackle the human genome after its successful application of large-scale DNA sequencing techniques to the genome of the roundworm, Caenorhabditis elegans.

The planned completion date for the roundworm genome is Dec. 31, 1998. NIH hopes the human genome will be sequenced by the year 2005. In late April, it was announced that sequencing of the yeast genome — which has more than 12 million base pairs of DNA — had been completed. Researchers here were part of the international collaboration to sequence the yeast genome, which provided the first sequence of an organism whose cells are like those of humans.

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**Quality Care, Shorter Hospital Stays**

Investigators here say that modifications in anesthesia and post-surgical care can shorten hospital stays without compromising quality of care in cardiac surgery patients.

Studying 422 patients who underwent bypass surgery, valve replacement surgery or bypass with valve replacement, the investigators found that minor changes in anesthesia, combined with an earlier, more aggressive activity regimen, shortened the average post-operative hospital stay by more than two days per patient.

The trial program was initiated as an attempt to improve patient outcomes and lower costs for both the patient and hospital. Shortening the length of stay lowered hospital costs by an average of $2,657 per patient; it also lowered readmission rates after surgery. Investigators found that 7.8 percent of patients who were sent home early were readmitted within 30 days. In those who stayed longer, the readmission rate was 16.2 percent.

The primary reason for reduced hospital stays, says lead investigator and surgical nurse Nancy Nickerson, was a change in anesthesia that allowed for earlier removal of breathing tubes after surgery. Prior to the early-release program, patients were kept on a ventilator for about 48 hours. That was reduced to less than 24 hours, and some patients’ tubes were removed in 10 hours or less.

Age, female gender, an irregular heartbeat after surgery, poor heart function and combined bypass and valve surgery were predictors of slower recovery.
Maps of soft-tissue changes in a residual limb are created by subtracting an image of the prosthesis-on condition from an image of the prosthesis-off condition. In red, soft tissue has been negatively displaced (pushed in). In yellow, soft tissue has been positively displaced (forced out) by the prosthesis.
Every year, approximately 60,000 Americans undergo the amputation of a lower limb. For them, the fitting of a prosthetic leg has been something of a trial-and-error proposition with weighty consequences for their comfort and activity levels.

For the dedicated prosthetists who help them, the creation of a prosthetic limb's socket to fit the patient's residual limb requires balancing intuition, experience and artistry with craftsmanship, subjective evaluations and patience. Often, a patient returns to the prosthetist many times to have a socket's shape fine-tuned, a process called rectification.

The problem has many layers. The prosthetist can see the patient's residual limb only when the socket is not in place, but contact between the socket and the limb alters the shape of soft tissue; the pressure of supporting weight alters it dramatically. Clear plastic models of a proposed socket help, but the bone obscured beneath soft tissue still must be accommodated precisely. And any assessment of pressure levels is an approximation. What's more, all of the pieces of this puzzle move in complex ways, bear various stresses and change over time.

The continuing success of the Prosthetic Fitting Systems Research Project promises a more quantifiable and repeatable way to fit a socket to a residual limb. Michael W. Vannier, MD, and his associates apply what Vannier calls “3-D, X-ray vision” to the process. The project's goal, he says, is to “provide a quantitative, image-based method of prosthesis fitting and to further the understanding of the biomechanical principles of a good-fitting prosthesis.”

BACKGROUND IMAGE: In p-version finite element analysis, a mathematical representation of a residual limb creates a mesh divided into various elements. When the computer applies a load at any point, quantifiable strains are created throughout the mesh.
It's an important goal, according to Jack Engsberg, PhD, associate professor of neurosurgery and director of the Human Performance Laboratory, because there has not been a systematic method for fitting prostheses, and "most patients are unaware of the fit they can achieve."

**IN THE BEGINNING**

The project began with a request from the National Center for Medical Rehabilitation Research for proposals to apply innovative technologies to rehabilitation science. Vannier, professor of radiology and one of the School of Medicine's most original developers of computer imaging applications, knew little about artificial limbs. But his experience as an engineer as well as a physician led him to believe that a prosthetic leg can be "optimized in the way any manufactured object can be."

Four years ago, with an initial grant in hand, Vannier's group at Mallinckrodt Institute of Radiology, including engineers Paul Commean and Kirk Smith, began to explore scientific methods for measuring the shape of residual limbs. They

By applying 3-D, X-ray vision to fit a socket to a residual limb, Michael W. Vannier, MD, hopes to design better fitting prostheses for lower-limb amputees.

built an optical scanner that acquired data from the surface of the residual limb, then computer processed and displayed the image in three dimensions. The computer model could be compared in shape with the residual limb itself and with traditional methods of building prostheses that entail making a plaster cast of the limb and then a mold for the inside of a socket.

The optical scanner made better precision and repeatability possible without touching the residual limb. Previously, measurements had been made with calipers and tape measures using landmarks established by the prosthethist. Such measurements were highly dependent upon the individual prosthetist, laborious and error-prone, Vannier says.

As the surface scanner's results were being validated, the researchers collected computed tomography (CT) scans. By using a CT scanner to gather the necessary data quickly, team members were able to add volumetric information and visualize not only the skin surface, but also the bone within the limb.

The volumes arrived at via the computer's interpretation of the CT data were verified by comparing them with results from the Archimedes water displacement test, in which the patient places his or her residual limb into a bucket of water, and the displaced volume is recorded. Results varied by 3 percent or less.

The CT scanner also provided the capability to differentiate the skin's surface, the soft tissue beneath and the bone in a patient's residual limb. More than 20 patients have been scanned to date, and Vannier says the experimental protocol calls for 50.

The CT scanner also can see through a socket to the limb beneath. By scanning the residual limb without a socket attached and then with a socket in place and applying engineering programs, the changes and relative pressures on the limb can be discerned.

Vannier says he first had difficulty comparing a limb with and without its socket because of registration problems incurred when the patient moved from the scanner table to put on the prosthesis. But, realizing that the bone in the limb did not change, he was able to realign complete images precisely...
by realigning the bone images. Subtracting an image of the limb without a socket in place from an image of the limb with the socket in place, and instructing the computer to add color, made the differences between the two conditions dramatically apparent.

In another inspired stroke, the researchers developed a method to evaluate the fit of a socket under load, such as might be experienced while walking. In the most sophisticated scanning procedure yet, the patient reclines on the scanner's bed wearing a body harness. A spring-loaded strap mounted to a scale extends around the foot of the socket onto the residual limb as the scan is made.

By scanning with pressure applied, the researchers gain otherwise unavailable insight into the changes that the socket must accommodate. Scans comparing loaded and unloaded conditions provide the range.

Which, Engsberg says, is just what is necessary. “We have to achieve precision, but still maintain absolute individuality for every patient,” he says. A previous attempt to improve the fit of artificial limbs by creating a library of basic shapes from which every socket could be rectified did not work. “It just wasn’t adaptable enough,” Engsberg says.

**FOR THE FUTURE**

An atlas can be created from the CT data in which a residual limb is electronically dissected into its parts: skin, fat, muscle, tendon and bone. The images can be rotated and viewed from any perspective, and they can be “unrolled” from their three dimensionality into two-dimensional maps. Vannier now is studying the mapping results and comparing them to end results to see if the maps are predictive of a good fit.

“By taking a fundamental, biomedical engineering approach, we came up with an easy way to see where the fit is bad and where it is good. We will end up building much better-fitting prostheses,” he says.

One of Vannier’s collaborators on the project, Barna Szabo, PhD, professor of mechanical engineering on the Hilltop Campus, applies a stress evaluation method he devised to take the mapping a step further. Szabo constructs mathematical replicas of complex objects in motion — previously they have been mechanical components used in cars and airplanes — to evaluate how they behave when they are stretched or compressed and to predict their behavior under stress.

Called p-version finite elements, the mathematical mapping permits researchers to predict the mechanical interaction between a residual limb and its prosthetic socket. The analysis is capable of accommodating the large soft-tissue deformations that occur as the bone remains stable and rigid. The result should be the best quality fit possible for the patient, Vannier says.

Engsberg says he may help to assess the quality of fit by evaluating the gait of volunteers in the study in the Human Performance Laboratory. There, scientists compare the loading of a patient’s prosthetic side with his or her non-prosthetic side by analyzing videotapes and recordings from platforms that register forces.

The entire computer application that interprets and displays the three-dimensional images and maps runs on a desktop workstation, and the total time required in a CT scanner is approximately 30 seconds. “The cost is minimal,” Vannier says. “Our goal has been to make the process practical and affordable, so that it can be available to everyone.”

Further in the future, he foresees the addition of a computer-aided manufacturing capability that accurately fabricates the socket of a prosthetic limb from the data acquired in a CT scanner. Such a machine would eliminate the need for subjective interpretations.

Engsberg says that prosthetists need not fear that a fully operational CAD/CAM technology would steal their work. “If prosthetists were freed from the job of rectification, they could use their time in the way they were trained and not have to worry about fit. They could help patients get the best appliances for their needs. A completely accurate way of manufacturing prosthetic limbs would only make the prosthetist more successful.”

At St. Louis’ Orthotics and Prosthetics Laboratory, resident prosthetist Jon Wilson says he believes that though some prosthetists may have to be retrained, the work always will center on evaluating patients’ histories and goals and recommending prescriptions. He looks forward to the time when the precision of the computer helps him to build more accurate, comfortable and functional limbs.

Editor’s note: The number of Washington University School of Medicine alumni and faculty who ascend to department head positions continues to grow. Clearly the school is fulfilling its mission of training, fostering and developing the next generation of medical leaders. Congratulations to Dr. Michael W. Vannier. At press deadline, we learned that he will assume responsibilities as head of radiology at the University of Iowa. He remains involved in ongoing research collaborations at Washington University.
June Hopkins was 13 years old when her mother told her she probably would never be able to have children.

Throughout her adolescence, physicians repeatedly warned June that her congenital heart defect would pose life-threatening risks in the event of a pregnancy. As a young adult, she was encouraged to consider a permanent form of birth control.

by Holly Edmiston
But Hopkins knew that having children was an experience she did not want to miss. "I kept thinking that somehow, somehow, they'd come up with something in the future and I'd be able to have a baby of my own," she says. Today, Hopkins, 35, has two children, and she credits School of Medicine cardiologist Patricia L. Cole, MD, with helping to make her motherhood a reality.

Cole, who is associate professor of medicine and co-director of the Barnes-Jewish Hospital Cardiac Catheterization Facility, specializes in women's cardiology. She began to study the issue of women and heart disease early in her career, and over the past decade has built an extensive practice made up largely of women. A portion of her practice concerns how the heart is affected by pregnancy.

"Many of the problems I see are preexisting conditions in women who would like to become pregnant or who already are pregnant, and their doctors are uneasy following them," Cole says. Because the field is relatively esoteric, many physicians shy away from the cases Cole finds most challenging. As a result, she often is called upon to offer a second opinion or consultation.

Patients generally are referred when they exhibit symptoms, or when their obstetrician has heard or seen something suspected to be a heart condition. Some patients arrive at her office in tears after being told by their cardiologists that they risk a 50 percent chance of dying if they go through a pregnancy. According to Cole, few conditions make pregnancy inadvisable for female cardiac patients. If the patient complies with and follows medical recommendations during pregnancy, the outcome is often successful, she says.
"The whole architecture of the heart changes remarkably during pregnancy — in thickness, in size, in function — then five weeks after delivery, it returns to normal."

Patient As Partner

"I fell in love with Dr. Cole," says Hopkins, who with her husband, Tony, and children, 4-year-old son, Cody, and daughter, Kendall, 11 months, lives in Collinsville IL. "She's intelligent, warm and friendly, so easy to talk to. She listened to my heart and read my charts and told me there was no reason why I couldn't have a baby and a normal, healthy pregnancy."

A metal valve that doctors implanted in Hopkins' heart at the age of 21 requires her to take warfarin, a blood-thinning drug that slows the clotting process. Warfarin is known to cause fetal abnormalities and thus precludes women who take it from becoming pregnant.

Through her obstetrician, Hopkins learned a pregnancy might be possible if she could switch to another drug during gestation. The substitute drug, heparin, can be used for short periods of time, but is unsuitable for long-term use because it depletes calcium. Unlike warfarin, an oral medication, heparin must be introduced into the body subcutaneously.

Hopkins conceived soon after receiving the go-ahead from Cole and the obstetrics high-risk team at then-Jewish Hospital. As soon as her pregnancy was confirmed, she was put on a heparin pump. Cole says women using the pump must be vigilant — it is cumbersome and requires continuous insertion of a needle into the abdomen throughout the pregnancy. In addition, the patient must undergo frequent blood testing to ensure that blood is appropriately thin.

Cole, who considers herself a partner in her patients' health care, says she admires and appreciates the dedication of patients like Hopkins. "June is my very favorite type of patient — one who says, 'I know there are risks, I trust you, we'll work together on this.'"

"I can really relate to Dr. Cole," Hopkins says. "As a woman and a mother, she is sensitive to my health concerns and was supportive of my desire to become pregnant."

While Hopkins was "ecstatic" about the pregnancies, her family was initially resistant, fearing for her health. They believed what they had been told for many years — that she was not likely to live through a pregnancy. Cole works to alleviate that sort of anxiety by sitting down with the family and thoroughly explaining procedures and any risks they may pose. "I say to them: 'Here's what's going on, here's what I predict, here's what the possible outcomes are, here's what I think the outcome is going to be, and here's the risk that you're going to take if you go through this with me.'"

As for Hopkins, she never had any doubts. "I knew it was going to be OK, that everything would work out," she says. "There was no way Dr. Cole would allow me to go through the pregnancy without a positive outcome."

Detecting The Problem

Cole — who earned her medical degree from Harvard University in 1981 — became interested in the area of women and heart disease as a fellow in medicine and cardiology at Brigham and Women's Hospital in Boston. There, she conducted research on the normal heart during pregnancy, sometimes using herself, then pregnant with her second child, as a subject. She continues to speak and write voluminously on women's cardiology issues. She and Washington University investigator Phyllis Stein, PhD, currently are conducting research on heart rate variability during pregnancy. The focus of her professional activity, however, remains clinical.

The cardiac issues her pregnant patients face run the gamut — including valve, muscle and artery problems. Some are congenital conditions that are recognized and treated before pregnancy occurs, some develop during pregnancy and some are present prior to pregnancy but the symptoms are unmasked by the changes of pregnancy. In Hopkins' case, she and a twin brother were diagnosed with
congenital heart murmurs. While her sibling outgrew the condition, Hopkins' heart began exhibiting subtle changes when she was in elementary school. Examination by a pediatric cardiologist revealed that her heart was enlarged and under strain. The aortic valve was neither developing normally nor opening and closing properly. Eventually, her parents were told, she would need to undergo surgery to replace the valve.

For the remainder of her childhood, Hopkins' heart was monitored closely. When she was 15, doctors surgically applied a patch to the valve, a temporary measure designed to help it open and close more efficiently and that would allow continued body growth. At 21, she underwent valve replacement surgery.

Cole says congenital heart problems are not uncommon in the patients she sees. Other conditions can be harder to diagnose, because the symptoms of heart problems and pregnancy often mimic one another. It can be difficult to determine whether a problem is occurring naturally as part of a normal pregnancy or if it is an indication that something is actually wrong with a patient's heart, she says. "The whole architecture of the heart changes remarkably during pregnancy — in thickness, in size, in function — then five weeks after delivery, it returns to normal," says Cole. "If you can figure out what those changes are, you can predict what should happen during pregnancy to a heart that has a structural abnormality." In addition, she says, the heart works harder during pregnancy, increasing both average blood volume and cardiac output by 30 to 50 percent. That extra workload can reveal previously obscured problems.

For example, if a patient unknowingly has mitral stenosis (a narrowing of the mitral valve), she might tire easily or experience shortness of breath, but attribute the symptoms to aging or some other cause, says Cole. If that same patient becomes pregnant, however, with a concomitant rise in both heart output and blood volume, the narrowed valve becomes unable to accommodate the increase and she begins to feel increasingly short of breath, experience leg swelling and may be unable to lie flat to sleep, all common symptoms of pregnancy. By carefully listening to a patient's heart, a murmur or other heart condition can be discovered, leading to a correct diagnosis, she says.

The majority of Cole's patients have more common problems, such as arrhythmias. "Most of what I do is reassure the patient and start them on proper medication, and then they're fine." Another frequent occurrence is mitral valve prolapse, an abnormality in which excess valve tissue billows out during heart contraction and causes a peculiar noise. Though many patients may experience shortness of breath and chest pain, the condition is not life threatening, she says.

Cole says she is fascinated with the physiology of the heart, particularly as it changes during pregnancy. She especially enjoys working with her pregnant patients, most of whom are healthy and who are often grateful for the support and guidance she offers them.

For June Hopkins, the wait, the risk and the work she endured were worth the effort. "When I see these two children I thought I'd never have, I feel blessed," she says.

For Cole, steering patients carefully through difficult pregnancies and helping them to fulfill their dreams brings both professional and personal satisfaction.

Some patients experience cardiomyopathy during their pregnancies, a condition in which the heart muscle does not pump properly. If the problem is due to the pregnancy (peripartum cardiomyopathy), there is a 50-50 chance that it will improve, says Cole. If the condition was caused by other factors, the pregnancy may bring out the symptoms and appropriate treatment can be administered.

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Patricia L. Cole, MD, co-director of the Barnes-Jewish Hospital Cardiac Catheterization Facility, says few conditions make pregnancy inadvisable for female cardiac patients.
David Schlessinger, PhD, and Giuseppe Pilia, MD, suggest that an interaction between glypican 3 and the growth-promoting substance IGF2 inhibits growth, either by directly lowering the concentration of free IGF2 or by promoting the binding of IGF2 to the IGF2 receptor, an event that leads to IGF's destruction.

In the ancient city of Cagliari, Italy, pediatrician Giuseppe Pilia encountered children whose faulty genes had misshaped their tissues and organs. In Ottawa, Canada, pediatrician Rhiannon Hughes-Benzie diagnosed two brothers as having a rare inherited overgrowth syndrome. In St. Louis, geneticist David Schlessinger was making a detailed map of chromosome X. Pilia, Hughes-Benzie and Schlessinger now have identified the gene for a disorder called Simpson-Golabi-Behmel Syndrome (SGBS) and found the first clue as to how the gene might work.

"The isolation of this gene provides an entree for studies of the master growth control mechanism by which tissues reach their normal size," says Schlessinger, a PhD and professor of molecular microbiology, genetics and medicine. "And because children with SGBS are at risk for embryonal tumors, studies of the gene's function may reveal a step that leads to cancer."
Mismatched Chromosomes

Cagliari lies on the southern coast of Sardinia, one of Italy’s remotest regions. Set in the Mediterranean more than 100 miles from the mainland, the island has developed a unique culture, with its own dialects, handicrafts and cuisine. Its isolation also has given it a unique disease profile, with high rates of disorders such as the thalassemias or "sea blood diseases."

Patients with such genetic disorders gravitate to the University of Cagliari, where they may become patients of Giuseppe Pilia, MD. Some of Pilia’s most frustrating cases are children with inherited disorders called dysmorphic syndromes, in which tissues and organs overgrow. "It’s very difficult to make a diagnosis without knowing which gene is involved," he explains. "But for most of these syndromes, there’s no such data."

The need for diagnostic tests led Pilia to search for faulty genes. Trading sandy beaches for the muddy Mississippi, Pilia became a postdoctoral fellow in 1990 in the Center for Genetics in Medicine, which Schlessinger directs.

The researchers were making a high-resolution map of chromosome X, which carries 2,000 to 3,000 of the estimated 100,000 human genes. When faulty, many of these can cause diseases, including Duchenne muscular dystrophy, color blindness and retinitis pigmentosa.

The center uses yeast artificial chromosome (YAC) technology to clone fragments of DNA for study. Developed at the School of Medicine and now used worldwide, the technology enables the DNA to be copied repeatedly inside yeast cells until there is enough material for analysis.

Pilia spent three years developing YACs containing DNA from a region called Xq26, near the end of X’s long arm. Then in a catalog from the National Institute of General Medical Sciences, he came across cultured cells whose chromosomes were faulty in this region. The cell lines had come from two females with an overgrowth syndrome.

In one cell line, a piece of X had traded places with a piece of chromosome 1. In the other, X had traded a piece with chromosome 16. Such misplaced pieces are called translocations, and the places where they rejoin are called breakpoints.

Surprisingly, such drastic errors are not always lethal because all of the misplaced genes can function except the one interrupted by the breakpoint.

Usually, females do not exhibit X-linked syndromes because they have two X chromosomes, in contrast to males, who have one X and one Y and therefore no backup copy of a defective X-linked gene. But the females with SGBS were using the X chromosome that had undergone the translocation and not the one with the normal gene.

Pilia realized that to produce the same syndrome the two translocations must disrupt the same gene. By locating the two breakpoints, he could track down the faulty DNA that gives rise to SGBS.

He suspected the females had SGBS rather than the overgrowth syndrome listed in the catalog, Beckwith-Weideman Syndrome (BWS). "Those cell lines were posted earlier, one in 1974," he

By Linda Sage

Giuseppe Pilia, MD, right, came to the School of Medicine’s Center for Genetics in Medicine, directed by David Schlessinger, PhD, left, to search for faulty genes that may contribute to the inherited childhood diseases he sees in his practice in Italy.
Canadian researchers Rhiannon Hughes-Benzie, MD, center, Jian Ying Xuan, MD, left, and Alex MacKenzie, MD, PhD, in the molecular genetics laboratory at the Children's Hospital of Eastern Ontario Research Institute.

This brother and sister are members of a Dutch-Canadian family, studied by Rhiannon Hughes-Benzie, MD, that has Simpson-Golabi-Behmel Syndrome. The boy, age 3, who has SGBS, is larger than his sister, age 4 1/2, who is of normal size.

explains. "The first report of an SGBS family was not made until 1976."

Males with SGBS grow to over 6 feet tall and may have distinct facial characteristics, enlarged internal organs, heart and skeletal abnormalities and more than two nipples. As children, they have an increased chance of developing Wilms tumor, a type of kidney cancer that is derived from embryonic cells. These symptoms suggest a fault in a gene that keeps tissue growth in check.

Looking at bands that appear when chromosomes are stained, Pilia determined the breakpoints were within Xq26. His task was to locate them exactly within the band, which spans about 10 million pairs of nucleotide bases.

He began to analyze DNA from one cell line in 1994. Using YACs and other tools, he located the breakpoint to 200,000 base pairs of Xq26 — a task comparable to narrowing the location of a house to a one-mile stretch of a 50-mile road. His next step was to find the house.

**SGBS Families**

In Canada, meanwhile, Rhiannon Hughes-Benzie, MD, a resident in medical genetics at the Children's Hospital of Eastern Ontario (CHEO), diagnosed the first of two Ottawa families with SGBS. The family's two boys were larger than expected for their ages, had enlarged internal organs and heart abnormalities, and one had a cleft lip and palate and an extra finger.

Hughes-Benzie made the diagnosis by using an Australian genetic database called POSSUM, which compared the physical features of the boys with those of more than 2,000 genetic syndromes.

Over the next few years, Hughes-Benzie and master's student Jian Ying Xuan, MD, worked together in the molecular genetics lab of Alex MacKenzie, MD, PhD, at the CHEO Research Institute to identify the location of the SGBS gene on the X chromosome. "We wanted to find a stretch of DNA that was identical in all the people who had the faulty gene," she explains. In 1993, the Canadian group published an abstract localizing the gene to a region of the chromosome that included Xq26.

That year, the Ottawa group first learned of Pilia's proposal to identify the SGBS gene in the cell lines with chromosome translocations. One of the lines was donated to the cell bank by Hope Punnett, PhD, an NIH geneticist at St. Christopher's Hospital for Children in Philadelphia. When Hughes-Benzie and Punnett reviewed the information, they determined that the female did have SGBS rather than BWS.

"We decided Giuseppe probably had the most rapid way to get at the gene, using the translocations," Hughes-Benzie says. So the Ottawa team and the St. Louis researchers began to collaborate to identify the gene that causes SGBS.

**Pinpointing The Gene**

Human genes are sparsely scattered along DNA, accounting for only about 3 percent of the total genome. Therefore, the 200,000 base pairs of DNA that Pilia had identified were likely to contain about four genes. Further analysis of this DNA identified a potential candidate for the gene underlying SGBS.

Using DNA from the site as a probe, Pilia identified the normal gene among copies of genes from human embryonic tissue. He also showed that the gene was interrupted in the two cell lines containing the translocations. Spanning 2,130 base pairs, the gene coded for a protein made of 580 amino acids.

The next step was to see whether the gene really did cause SGBS. Using DNA samples from three of the SGBS families in the Ottawa database, Pilia showed that
the genetic error in the males affected the same gene as that disrupted by the translocations, though the error was just a single spelling mistake in the nucleotide code words. "This was the formal proof that the gene we had identified in the cell lines was the gene responsible for the mutation in those families," Pilia says.

Using Pilia's probes, Hughes-Benzie began to test the other DNA samples. "The deletions now have been detected in affected individuals in seven unrelated families," she says.

As added evidence, Pilia showed that the gene is active mainly before birth in mice, beginning its work exactly as tissues and organs start to form. He also found that it is expressed primarily in those tissues and organs that overgrow in SGBS patients. "Because these tissues overgrow when this gene is faulty," he says, "the normal gene somehow must suppress the growth of those tissues."

**A New Growth Regulator?**

After sequencing the SGBS gene, Schlessinger and Pilia compared their data with sequences in GenBank, a database maintained at the National Center for Biotechnology Information in Bethesda MD. The gene proved to be similar to a rat gene that codes for a glypican.

Glypicans are bulky sugar proteins found on cell membranes, but their function is unknown. Moreover, they have not previously been associated with any medical condition. "So this will open up enormous interest in this class of proteins," Schlessinger says.

The researchers named the new gene glypican 3. They obtained the first clue to its function by exploring the suggestion that BWS, whose symptoms resemble those of SGBS, might result from a problem with a substance called insulin-like growth factor or IGF.

IGF was discovered at the School of Medicine by William Daughaday, MD, former Irene E. and Michael M. Karl Professor in Metabolism. In 1957, Daughaday found that serum contains a growth-promoting substance induced by growth hormone. Based on his observations, other scientists later isolated the protein, now called IGF1. A related protein that stimulates growth in the fetus is called IGF2.

Using antibodies he made to glypican 3 protein, Pilia found that there might be a connection between IGF2 and overgrowth syndromes because the growth factor was able to interact with the glypican. "The fundamental mechanism we are proposing is that glypican 3 ordinarily limits the activity of IGF2 by binding to it or promoting its breakdown," Schlessinger explains. "When a person can't make glypican 3 because of a faulty gene, there is too much IGF2 activity in certain tissues, which overgrow, giving rise to these syndromes."

Now that the glypican gene is in hand, SGBS can be distinguished from BWS, which results from a faulty gene somewhere on chromosome 11. "These families want to know what affects them and their children," Hughes-Benzie says. "Now we can offer a definitive test."

Once patients know they have SGBS, they can be screened for heart defects and tumors. "This discovery may help all children with embryonic tumors, not just those with SGBS," Hughes-Benzie says, "because overgrowth of tissues and the production of tumors may share a similar mechanism."

Back in Cagliari, Pilia is generating mice that lack glypican 3 so he can learn more about the gene's normal function. He also intends to apply the techniques he learned in St. Louis to other diseases, such as asthma, that are prevalent in Sardinia.

"David Schlessinger created an environment in which I was able to make a lot of useful mistakes and learn from them," he says. "He is a formidable maestro — able to give direction while infusing courage and respect for one's own potential."
Implant Improv

I discerning ear — three distinct words. But to as many as 4 million Americans who have severe sensorineural nerve hearing loss, they may be indistinguishable.

For years, the hearing handicapped in this population — who suffer moderately severe to severe nerve deafness — have had to rely on conventional hearing aids. But conventional aids, which can be worn either outside of the ear or inside the ear canal, produce additional distortion of the amplified sound which adds to distortion resulting from existing serious nerve damage.

by Kleila Carlson

The electromagnetic transducer's battery and microphone are worn behind the ear, much like a conventional hearing aid. The middle ear implant operates with an electromagnetic transducer that takes the sound that is delivered to the microphone, converts it into a vibratory pattern and directly vibrates the bones of the middle ear.
"Imagine listening to a sentence and missing two key words, and then trying to figure out what was said. That gives you an idea of how difficult it is for these people to understand what is going on around them," says John M. Fredrickson, MD, Lindburg Professor and head of the Department of Otolaryngology.

Fredrickson and colleagues Barbara A. Bohne, PhD, Michael Valente, PhD, Margaret W. Skinner, PhD, and medical research engineers Doug Miller and Maynard Engberston, working with Otologies, a St. Louis company, have developed an implantable device to help those whose hearing has been damaged. Now, after a lengthy study in animals and a short-term human trial involving two patients, the researchers are preparing to go before the U.S. Food and Drug Administration in the hope of launching a clinical trial here before the end of the year. After a successful initial trial, a multicenter trial will follow at five sites around the country.

"Our results have been very encouraging," Fredrickson says of the studies that already have taken place. "Our implant provides a marked improvement in sound quality and an improvement in speech discrimination in both noisy and quiet environments."

While the effectiveness of conventional hearing aids has greatly improved, Fredrickson says pronounced problems still exist with feedback and amplification. Feedback occurs when sound bounces off the eardrum, travels back to the hearing aid amplifier and is re-amplified, causing a squealing noise. Even before the squeal occurs, the amplified sound becomes distorted.

Impedance mismatch also can cause distortion, particularly in high frequencies. It occurs when the amplification of sound through air is translated to a fluid motion in the inner ear.
The middle ear implant that Fredrickson has devised operates with an electromagnetic transducer that takes the sound that is delivered to the microphone, converts it into a vibratory pattern and directly vibrates the bones of the middle ear. The probe tip of the implant has direct contact with and drives the middle ear's three tiny bones — the malleus, incus and stapes — which transmit sound from the tympanic membrane to the oval window.

"We directly couple the input of the signal mechanically to the incus, and since there is no speaker there is essentially no feedback as a source of distortion," Fredrickson says. "Also, there is improved impedance (resistance) matching because the ossicular chain is being mechanically driven."

**Something Better**

Fredrickson says the majority of the 25 million Americans who are hearing impaired can be satisfactorily treated with traditional hearing aids. The electromagnetic transducer he has spent the last decade perfecting offers something better than conventional hearing aids for those with moderately severe to severe nerve hearing loss. At this time, he says, it is one of three types of middle ear implant being investigated.

A piezoelectric device, in which a crystal is placed against the middle ear's innermost bone, the stapes, causing it to vibrate, is under investigation in Japan. Although it is suitable for people with mild to moderate hearing loss, Fredrickson says it fails to produce enough volume for those with more severe hearing problems. An electromagnetic coil, which involves placing a magnet between the incus and the stapes, along with a coil in the external ear canal, is also being studied. Fredrickson says the coil is uncomfortable and can cause infections and wax buildup, and it does not generate enough power to treat the target population.

"To our knowledge, ours is the only transducer which produces sufficient energy to address the hearing needs of patients with moderately severe and severe sensorineural hearing loss. We have developed a unique device for a unique population — a population that requires something better than what is currently out there," says Fredrickson.

The electromagnetic transducer's battery and microphone are worn behind the ear, much like a conventional hearing aid, and an external coil sends a signal across the skin to the implanted subcutaneous receiver. The receiver picks up the signal, transposes it to the transducer, and the transducer vibrates the ossicular chain.

Surgery to implant the device requires an incision behind the ear and the drilling of two small holes, approximately 8 to 9 millimeters in diameter. One hole is for observation and the other is to position the transducer. Once the incus is exposed, a laser is used to carve out a small dimple so that it can receive the transducer's probe tip which is left there to heal, a process which takes about five weeks.

"After the incision heals and the implant is operating, we should have an immediate hearing improvement," Fredrickson says. Should the implant malfunction, it can be taken out and re-implanted with no harm to the patient, he adds.

Fredrickson is encouraged by research data that have been gathered. Of the two patients temporarily implanted with the device, one had "very significant" improvement in word discrimination and the other had "significant" improvement. Both patients had moderately severe to severe nerve hearing loss in both ears.
Word discrimination, a measurement of speech understanding, is gauged by having patients repeat words that have just been recited to them. People with severe hearing loss generally have discrimination scores varying from about 10 to 60 percent, meaning that they can repeat words they hear accurately 10 to 60 percent of the time.

"Research has shown that if the discrimination score can be increased by even a small amount, perhaps 5 to 10 percent, a patient's understanding of speech increases far greater than what one would imagine."

In the animal study, researchers monitored acoustic responses by examining various auditory-evoked potentials — one of which is the auditory brain stem response. Another test, called distortion product otoacoustic emission, showed that the transducer was faithfully stimulating the inner ear with the predetermined intensity and frequency of sound being delivered to the animals.

"We obtained excellent auditory responses during the course of the implantation in the chronically implanted animals," says Fredrickson. "We have been able to demonstrate that the implantable middle ear transducer delivers frequency-specific and intensity-specific information to the cochlea with a high degree of fidelity. That's really the key issue."

Who Can Benefit?

Although severe sensorineural hearing loss can occur in the young, Fredrickson anticipates that most of those who will be helped by the device will be over the age of 50.

"We will be dealing primarily with older people who have been exposed to a lot of noise during the course of their lifetime. People who were exposed to rifle and artillery fire and people in industry and agriculture who are around machinery — particularly those who were involved in these areas before hearing protection devices were developed — have significant hearing loss. Today, aging seems to be less of a factor than noise-induced hearing loss."

Fredrickson says the normal ear can be harmed by far less noise than one might think. Just eight hours of exposure to noise levels of 80 decibels — which is about 20 decibels higher than normal conversation — will cause damage. "Someone who is in a moderately noisy environment, if they are in it for a very long period of time, will sustain damage to their hearing," he says. "People don't have to be around jet engines. All they have to do is attend rock concerts or sports venues and the eventual damage can be significant. If you come out with your ears ringing or humming, that means you have suffered some damage."

In the spectrum of hearing loss, which goes from mild to severe, a 25 to 40 decibel loss is mild, a 40 to 55 decibel loss is moderate, a 55 to 70 decibel loss is moderately severe and a 70 to 90 decibel loss is severe. Anything above 90 decibels is considered profoundly deaf and can only be treated with a cochlear implant.

"The maximum output level required by a device to treat patients in the moderately severe to severe group, our target population, ranges from 105 decibels to 135 decibels. To our knowledge, the only implantable device currently being investigated that can do this is our device," says Fredrickson.

The implant costs more than a conventional hearing aid because surgery is involved, but Fredrickson believes that its advantages will outweigh any potential drawbacks. When technology has advanced sufficiently, he says, he would like to implant the entire device — including the battery and microphone — so nothing is seen externally.

"Needless to say, we are excited," says Fredrickson. "Conventional hearing aids don't provide sufficient help for our targeted patient population. These people are struggling along, trying to adapt to their social and work environments with little satisfaction, looking for something better. We hope to be able to provide something better with our implantable device."
THE annual Match Day took place on March 20 with 111 of the 118 graduating medical students participating in the National Residency Matching Program.

Of the participants, 60 percent received residency positions at their first choice of institution and 86 percent matched one of their top three choices. The eight students who did not take part found positions independent of the NMMP or chose not to take residencies immediately.

Primary care specialties of internal medicine, pediatrics and family practice captured the interest of 62 students. Family practice attracted eight students this year, down two from last year. Obstetrics-gynecology was fourth in popularity, attracting six students, followed by orthopaedic surgery, radiology and pathology, each of which attracted five students.

Twenty-eight of the new physicians will remain in St. Louis, with 24 at Washington University Medical Center institutions. Other popular destinations were California (12), Massachusetts (9), Pennsylvania and Minnesota (6) and Washington (5).

California
Sacramento
University of California-Davis
  - General Surgery
  - Rose Baghdady
  - Internal Medicine
  - Christine Tsou
San Diego
University of California-San Diego
  - Internal Medicine
  - Priya Bhursi
San Diego Naval Hospital
  - Pediatrics
  - Pamela Frei
San Francisco
University of California-SF
  - Internal Medicine
  - Deborah Linde
  - Michael Ohl
  - Pediatrics
  - Sherry Meng
Long Beach
Long Beach Memorial
  - Family Practice
  - Diane Jerng
Los Angeles
UCLA Medical Center
  - Neurosurgery
  - James Forage
  - Internal Medicine
  - Jeffrey Hadassal
  - Family Practice
  - Judith Kraft

Otolaryngology
  - Ellie Maghami

Colorado
Denver
University of Colorado
  - Internal Medicine
  - Christopher Ricca
  - Pediatrics
  - Scott Sagel

Connecticut
New Haven
Yale-New Haven Hospital
  - Ob-Gyn
  - Yuen M. Chau
  - Internal Medicine-Preliminary
  - Stacey Englander

Florida
Gainesville
University of Florida-Shands Hospital
  - Internal Medicine
  - Richard Handler
Miami
Mt. Sinai Medical Center
  - Surgery-Prelim.
  - Michael Salzhauer
Tampa
University of South Florida
  - General Surgery
  - James Huang
Ophthalmology
Ivan Tarle

Georgia
Atlanta
Emory University School of Medicine
Neurosurgery
Prithvi Narayan
Ob-Gyn
Terence Young

Massachusetts
Boston
Brigham & Women's Hospital
Internal Medicine
Joshua Cooper
Anand Dighe
Emergency Medicine
Hilary Cranmer
Beth Israel Hospital
Internal Medicine
Scott Gilbert
David Loren
Children's Hospital
Pediatrics
Christopher Hug
Massachusetts General Hospital
Internal Medicine-Primary
Jennifer Ligibel
Lawrence
Greater Lawrence Family Health
Family Practice
Brenda Brischetto
Worcester
University of Massachusetts Programs
Family Practice
Jeffrey Baxter

Maryland
Baltimore
Johns Hopkins Hospital
Surgery-Preliminary/
Otolaryngology
Alyson Buckner
Johns Hopkins Bayview
Internal Medicine-Preliminary/
Johns Hopkins Hospital
Neurology
Gregory Mathews
University of Maryland
Internal Medicine-Preliminary
Howard Rogers

Michigan
Ann Arbor
University of Michigan
Internal Medicine-Preliminary
Scott Lee
Internal Medicine
Amit Shah
Detroit
Grace Hospital
Emergency Medicine
Harlan Hodges

Minnesota
Rochester
Mayo Graduate School of Medicine
Physical Medicine & Rehabilitation
Craig Carmichael
Robert Yang
Internal Medicine
Andrew Greenland
Michael Mahr
Internal Medicine-Preliminary/
Neurology
Laura Greenland
St. Paul
St. Paul-Ramsey Medical Center
Family Practice
Randall Pass

Missouri
Columbia
University Hospital & Clinics
Family Practice
Kimberly Schiel
St. Louis
Barnes-Jewish Hospital
Internal Medicine
Timothy Capstack
Penelope Ewbank
Kevin Korenblat
Ryland Melford
Internal Medicine-Preliminary
Lori Clements
John Lim
Veronica Weston
Laboratory Medicine
Chris Ho
Orthopaedic Surgery
Steven Klepps
Pathology
Wenhung Wang
Psychiatry
Tanya Haussler
David Montani
Radiation Oncology
Joseph Aronovitz
Imran Zoberi
Radiology-Diagnostic
Lori Clements
Scott Lee
John Lim
Surgery-Preliminary
Sam Bhayani
James Lu
Vrijesh Tantuwaya
St. Louis Children's Hospital
Pediatrics
Kara Arvin
Kimberly Goldberg
Kelly Heidenreich
Karen Ruecker
Nicole Willeumier
St. John's Mercy Medical Center
Pathology
Barry Cordes
Family Practice
Catherine Stocklin
Ob-Gyn
Heidi Sturtevant
St. Louis University
Pediatrics
Jenny Sou
Washington University
Ophthalmology
Heather Harvey
Neurology
James Lu
Urology
Sam Bhayani
Neurosurgery
Vrijesh Tantuwaya

New Mexico
Albuquerque
University of New Mexico School of Medicine
Pediatrics
Suman Malempati

New York
New York
The New York Hospital
General Surgery
Julie Miller
Internal Medicine
Robert Minutello
Monika Shah
St. Luke's-Roosevelt
Orthopaedic Surgery
Christopher Chen

North Carolina
Chapel Hill
University of North Carolina Hospital
Internal Medicine-Prelim.
Heather Harvey
Durham
Duke University Medical Center
Internal Medicine
Suzanne Boyer
Sally York

Ohio
Cincinnati
University of Cincinnati Hospital
Pediatrics
Pamela Beahm

Oregon
Portland
St. Vincent Hospital
Internal Medicine
Timothy Bateman
Oregon Health Sciences University
Pediatrics
Andrea Blum
Internal Medicine-Primary
Heather Burgin

Pennsylvania
Philadelphia
Hospital of Univ. of Pennsylvania
Internal Medicine
Matthew Kim
David Serlin
Alison Wackoff
Pathology
Bruce Sachais
Ilka Warshawksy
Reading
Reading Hospital Medical Center
Ob-Gyn
Abby Beall

Rhode Island
Providence
Rhode Island Hospital
Pediatrics
Elizabeth Maranzano

Tennessee
Chattanooga
University of Tennessee College of Medicine
Transitional
Ivan Tarle

Texas
Dallas
University of Texas Southwestern Medical Center
Internal Medicine
Thomas Barker
Christopher Solaro
Houston
Baylor College of Medicine
Pediatrics
Eric Anderson
Katherine Shiue

San Antonio
Lackland Air Force Base
Internal Medicine
Steven Kindsvater

Utah
Salt Lake City
University of Utah Affil. Hospitals
Pediatrics
Mike Leonis

Virginia
Charlottesville
University of Virginia
Charlottesville
Pediatrics
Thomas Hayne

Washington
Seattle
University of Washington
Otolaryngology
Rosalia Fonseca
University of Washington Affiliated Hospitals
Internal Medicine
Chyi Song Hsieh
Internal Medicine-Preliminary/Radiology-Diagnostic
Eugene Tong
Virginia Mason Hospital
Transitional
Robert Yang
Tacoma
Madigan Army Hospital
Internal Medicine
Eric Shry
Yakima
Central Washington Family Medicine
Family Practice
Neil Olsen

Wisconsin
Madison
University of Wisconsin Hospitals/Clinics
Orthopaedic Surgery
Robert Bane
Radiology-Diagnostic
David Neidhart
Ob-Gyn
Linda Neidhart

Third World Country
Year of Medicine
Hamid Ehsani
Seven Honored With Awards

The 1996 Reunion Award recipients, front L to R: Larry J. Shapiro, MD '71; Claire Anderson, MD '71; William H. Danforth, MD; and Gladden V. Elliott, MD '46; back, L to R, Lowell A. Gess, MD '51; Gordon W. Philpott, MD '61; and Louis P. Dehner, MD '66.

Alumni/Faculty Awards

Claire Anderson, MD, is professor of radiology, radiologist in the chest section at Mallinckrodt Institute of Radiology, and consulting radiologist at Barnes-Jewish Hospital, St. Louis Children's Hospital and the Veterans Administration Hospital. Noted for her excellent teaching skills, Anderson received the Teacher of the Year Award in 1983 and has been faculty radiology adviser since 1977. She directed the MIR resident program in diagnostic radiology from 1988-1992.

Lowell Arthur Gess, MD, is an ophthalmologist and an ordained minister of the United Methodist Church who has devoted his career to medical missionary work in Africa. He designed and copyrighted his own intraocular lens and made the technology available to millions of people in West Africa. He also taught and demonstrated surgery for extracapsular cataract extractions with intraocular lens implantations in Kenya, Nigeria, Ghana, Haiti, and Zimbabwe.

Larry J. Shapiro, MD, is W.H. and Marie Wattis Distinguished Professor and chairman of the Department of Pediatrics at the University of California, San Francisco School of Medicine. He has been repeatedly recognized for his research in genetics and cystic fibrosis. The National Institutes of Health granted Shapiro the Research Career Development Award, and the Western Society for Pediatric Research gave him the Ross Young Investigator Award.

Gordon W. Philpott, MD, is the Harry Edison Professor of Surgery and professor of radiology. He was chief of surgery at the former Jewish Hospital for 11 years. Since 1988, he has been the principal investigator for a number of grants from the National Institutes of Health. His recent research has focused on colon cancer, specifically on identifying the best reagent for tumor detection.

Gladden V. Elliott, MD, is a former clinical professor of radiology at the School of Medicine at the University of California, San Diego. He helped to develop a standard scale for determining appropriate fees for radiological services in inpatient settings which eventually was adopted by the State of California. He was an early advocate for non-smoking legislation, leading an effort in 1985 to set a goal for a tobacco-free public society by the year 2000.

William H. Danforth, MD, is chairman of the board of trustees of Washington University and co-chairman of the board of Barnes-Jewish Hospital. He retired in 1995 from the chancellorship of the university after 24 years of service. He led the university to national and international recognition, moving it forward in quality and prestige. During his tenure, applications to undergraduate school increased more than 50 percent, nearly 60,000 degrees were granted, and 10 Nobel laureates and two Pulitzer Prize winners were named from the University.
Members of the Class of 1971 reminisce at the welcoming cocktail party: From left: David Merrell, MD; Carla Beechie, MD; Elna Phelan, MD; reunion class gift chairman Richard Blath, MD; Phillip Hertzman, MD; James Oda, MD; reunion class social chairman Carlos Daughaday, MD; and Claire Anderson, MD.

Classmates from 1961 at the reunion banquet. Seated, from left, are Judith Pfeffer-Hurwitz, MD; Aryeh Hurwitz, MD; Macey Colvin; Michael Colvin, MD; and Ellen Blaustein. Standing, from left, are Richard Cooper, MD; Andrea Cooper; and Mordecai Blaustein, MD.

Harriet Smith Kaplan, MD ‘56, and Melvin Kaplan, MD.

The music of the “Hot Docs” moves the banquet guests to dance.

WUMCAA President-elect Julian C. Mosley Jr., MD ’72, after having accepted the gavel from Richard A. Blath, MD.
Robert Kiyomura, MD, ’76, with Class of 1976 reunion social chairman John Schilling, MD, and Linda Schilling at their class dinner.

Helen Marie Freund and Class of 1936 reunion social chairman Lawrence Aronberg, MD, with Bette and Fred E. Cooley, MD ’36.

Dean William A. Peck, MD, recognizes Richard Blath, MD, for his service as president with a gift.

Benjamin Milder, MD ’39, (standing) greets Eugene Bricker, MD ’34, at the reunion banquet. At right, is Phyllis (Mrs. Benard) Adler.

Richard Cooper, MD ’61, a guest speaker, chats with Dean William A. Peck, MD, at the Scientific Program.

Chancellor Mark S. Wrighton, PhD, greets Robert C. Petersen, MD ’56, while Bernice Petersen, left, and Sondra Orup and Hans I. Orup, MD ’56, look on.
A group of reunion-goers visits the Human Genome Sequencing Center.

Matthew Arquette, MD, Clark West, MD, and reunion class social chairman Michael Korenfeld, MD, all from the Class of 1986.

Richard A. Blath, MD '71, WUMCAA president, left, and Willard B. Walker, MD '46, social chairman for the 50th reunion class, welcome Scott Gilbert, president of the Class of 1996, and his classmates into the Alumni Association at the reunion banquet.

Washington University Chairman of the Board of Trustees William H. Danforth, MD, greets reunion class gift chairman Lt. Gen. Kenneth E. Pletcher, MD '36. Muzette Pletcher is to the left of her husband.

Members of the Class of 1951 meet at the welcoming cocktail party. From left: Walter A. German Jr., MD, and Taney German; Roscoe Vaughn, MD, and Beck Vaughn; James H. Dunlevy, MD, and Becky Dunlevy.

James C. Folsom, MD '46, enjoys his retirement and his reunion.
Dean William A. Peck, MD, right, presents the Alumni/Faculty Award to reunion class gift chairman Gordon W. Philpott, MD ’61, as Richard A. Blath, MD ’71, looks on.

From left, Willard B. Walker, MD ’46; Tosca Schaberg; Class of 1966 reunion social chairman Kevin B. Schaberg, MD; and Paul O. Hagemann, MD ’34, at the reunion banquet.

Larry Shapiro, MD ’71, (second from right) is congratulated by his parents, Philip and Phyllis Shapiro, left, Philip Dodge, MD, and his daughter, Jennifer Shapiro, on receiving the Alumni Achievement Award.

From left, Erwin R. Rabin, MD; Mickey Rabin; Lynn Lyss; Carl A. Lyss, MD; Shirley Hudgens; and reunion social chairman Richard W. Hudgens, MD, enjoy their Class of 1956 dinner.

Classmates from 1946, Robert E. Funsch, MD; Gilbert L. Chamberlain Jr., MD; and Albert P. Rauber, MD.

Elizabeth (Mrs. William H.) Danforth with Class of 1951 reunion social and gift chairman Marvin E. Levin, MD, and Barbara Levin.
From left, Class of 1941 reunion social chairman, Vergil N. Slee, MD, with classmates Kenneth Koerner, MD; Harold E. McCann, MD; and spouses Helen McCann and Beth Slee.

Classmates from 1941, Samuel E. Schechter, MD; Samuel W. Gollub, MD; and Joseph L.B. Ivins, MD.

Randy Farmer, right, assistant vice chancellor for medical alumni and development, presents Nicholas H. Nauert Jr., MD '46, with his Bachelor of Arts diploma. Nauert was admitted to the School of Medicine without receiving an undergraduate degree because of the urgent need for physicians during World War II.

At the Class of 1966 dinner, from left, are Joseph F. Ruwitch Jr., MD; Ben R. Mayes Jr., MD; Daniel J. Leary Jr., MD; Pat Leary; Herbert T. Abelson, MD; and Charles K. Harmon, MD.

Reunion class social chairman Michele Kemp, MD '81, (standing) greets classmates Suzanne Lee, MD, seated left, and Alice Ann Gricoski, MD.

Baron Harper, MD '86, and Cheryl Harper at the luncheon seminar on financial planning for retirement.
Young scientists made a strong showing at the 49th annual Greater St. Louis Science Fair in April. Among the science fair's 10 finalists were four participants in the School of Medicine's Young Scientist Program. They are, from left, Loan Tran, Susan Lewis, Norma Todd and Bart Bartlett, who was a division winner. The Young Scientist Program, started in 1991, was designed to educate, focus and inspire St. Louis high school students interested in science. Tran is a student at Roosevelt High School, Todd and Lewis attend Gateway High School and Bartlett is a student at Metro High School.
Julie Miller, left, and Rosália Fonseca beam as they prepare for commencement exercises, held on May 17 at the Hilltop Campus. The School of Medicine conferred 101 MD degrees, 15 MD/PhD degrees and two MD/MA degrees.