Got calcium in the wrong places?
**House call** Pebbles, a giant tortoise at the Saint Louis Zoo, gets checked out by John P. Kirby, MD, far right, assistant professor of surgery and director of the School of Medicine's Wound Healing Program. Kirby treated a wound on Pebbles' shell, with assistance from Linda Stamm, RN, MSN, far left, and Laurel Wiersema-Bryant, RN, MSN, nurse practitioners at Barnes-Jewish Hospital, and Zoo veterinarian Michael Adkesson, DVM.
Front Door

The Farrell Learning and Teaching Center now serves as the School of Medicine's main venue for medical education.

medicine.wustl.edu/fltc
**Farrell Learning and Teaching Center**

Located in the heart of the Washington University Medical Center, at the intersection of Euclid and Scott avenues, the Farrell Learning and Teaching Center serves both medical and graduate students with a variety of modern teaching environments.

- With the latest technology throughout the building, every seat in the lecture halls is wired with power and data connections.
- New spaces emphasize small group learning.
- A clinical skills instruction suite allows interactions with standardized patients.

**Giving Opportunities**

- Prominent naming opportunities are available throughout the building, starting at $25,000.
- Annual Fund gifts, at any level, will support this important addition to medical education.

Contact the Office of Medical Alumni and Development at (314) 286-0086.
Hearing Hairs

The study of hair regeneration genes in chicks may allow researchers to one day devise treatments for hearing impairment in humans.

Origins of Alzheimer’s

A new method of measuring amyloid beta, a protein found in high levels in Alzheimer’s patients, may shed new light on the condition.

No Bones About It

Calcium, the body’s friend in the formation of strong bones, can become an enemy when it deposits in the vascular system.

Back on Your Feet Again

Tarsal tunnel release surgery relieves pressure on the tibial nerve — restoring one young man’s ability to walk.

COVER Vascular calcification, the hardening of blood vessels and valves, can have serious health consequences. Dwight A. Towler, MD, PhD, director of the Division of Bone and Mineral Diseases, is researching the processes that create these bone-like deposits in arteries. For more on this story, please turn to page 16.

PHOTO BY TIM PARKER
In recognition of great leadership:  
The Danforth Campus

Campus designation honors extraordinary dedication

In recognition of the role that William H. (Bill) Danforth, Life Trustee and chancellor emeritus, his family and the Danforth Foundation have played in the evolution of Washington University in St. Louis, the Hilltop Campus was officially renamed the Danforth Campus on September 17, 2006.

"Bill Danforth has been one of the most respected leaders in higher education," says Chancellor Mark S. Wrighton. "He will be remembered as the man who, together with his late wife, Elizabeth, loved the university and loved working hand-in-hand with faculty, students and alumni to increase its strength and the contributions that only a university can make to modern society."

Danforth joined the medical school faculty in 1951, rising through the ranks to become vice chancellor for medical affairs in 1965 at age 39. He was named successor to retiring Chancellor Thomas Eliot in 1971, serving in that position until his own retirement on June 30, 1995.

During his 24 years as chancellor, Danforth oversaw the establishment of 70 new faculty professorships, built a $1.72 billion endowment, tripled the number of scholarships for students and completed the most successful fund-raising campaign in U.S. higher education.

By the time Danforth retired and was elected chairman of the board, his accomplishments were recognized nationally. He had set the course for the future of the university and completed its transition from a local college to a national research university, recruiting talented students and faculty from around the world.

Nearly 60,000 students graduated during his chancellorship, and retention of undergraduate students and the recruitment of minority students increased significantly. He became one of the longest-serving university chancellors or presidents in American higher education.

In addition to the Danforth family, the university is grateful to the trustees of the Danforth Foundation, which included Bill, Don and Jack, and their father and grandparents, for important financial support.

"The Danforth Campus will be a tribute to a man, a family and a foundation — all of whom envisioned a world-class future for this institution and worked to make it happen," says Wrighton. "In this way, the Danforth name will live prominently, forever, at Washington University in St. Louis."
Multidisciplinary approach to the diagnosis, treatment and care of diabetes

New center focuses on patient education

Patients managing diabetes now can get full diagnostics, treatment and education in one place — the Washington University Diabetes Center at Barnes-Jewish Hospital.

Located on the 13th floor of the Center for Advanced Medicine, the Diabetes Center provides a new group-care and patient-education approach for patients with type 1 or type 2 diabetes, says Garry S. Tobin, MD, associate professor of medicine and medical director of the center.

Longtime and newly diagnosed patients will have access to the latest technology, treatments and clinical research at the center. In addition, through individualized instruction and small-group sessions on topics such as nutrition counseling, carbohydrate counting, insulin self-management and insulin pumps, patients will learn how to maintain better control of their blood sugars.

Along with Tobin, the staff will include American Diabetes Association-certified nurse educators, registered dietitians, advanced-practice-ADA-certified nurses, a clinical nurse manager and support staff, as well as other physician members of the Diabetes Center.

“The Diabetes Center is a way for primary care physicians and their patients to get support from endocrinologists and other allied health specialists in diabetes treatment,” says Tobin. “Patients can seek services from an institution recognized as a national leader in the area and from specialists who can manage complex cases or complications as a team with their referring physicians.”

The Diabetes Center's staff is also developing and implementing inpatient protocols for newly diagnosed or long-term patients with diabetes to help gain or maintain diabetes control when they are admitted to Barnes-Jewish Hospital.

“We've tapped into the brainpower of a panel of medical advisers representing the power and skills of both Washington University and Barnes-Jewish Hospital to develop these inpatient protocols,” Tobin says. “The support of the dedicated and terrific nursing staff has made this process a success for the center as well as for patient care.”

Harbour is distinguished professor

J. William Harbour, MD, has been named the Paul A. Cibis Distinguished Professor of Ophthalmology and Visual Sciences. Established in 2000 by a donor who wishes to remain anonymous, the professorship honors the late Paul A. Cibis, MD, a seminal figure in the history of the department.

Harbour, who also is associate professor of molecular oncology and of cell biology and physiology, specializes in the diagnosis and treatment of eye tumors. He has been involved in cancer research since 1988 when he was the first author of a groundbreaking study that appeared in the journal Science describing changes in the tumor suppressor gene that cause the childhood eye cancer called retinoblastoma.

Harbour also studies ocular melanoma, the most common form of eye cancer in adults, and he is working to develop a clinical test that can be used to guide the management of patients with the disease.

He also directs the Ocular Oncology Service at the School of Medicine. Through the service, housed in the Barnes Retina Institute, Harbour is actively involved in the training of medical students, residents and fellows.
School of Medicine affiliate hospitals rank among the nation’s best

Washington University School of Medicine partners Barnes-Jewish Hospital and St. Louis Children's Hospital earned high honors in the 2006 U.S. News & World Report Honor Roll of "America's Best Hospitals."

Barnes-Jewish garnered the No. 8 spot in an overall ranking of America's medical centers, while Children's ranked No. 14 on the list of pediatric hospitals.

Barnes-Jewish and its physician partners at the School of Medicine are the only St. Louis-area hospital and medical institution to make this year's list. Barnes-Jewish Hospital was further honored by earning high marks in 14 specialties: endocrinology; ear, nose, and throat; kidney disease; neurology and neurosurgery; respiratory disorders; urology; heart and heart surgery; ophthalmology; orthopedics; digestive disorders; psychiatry; rheumatology; cancer; gynecology.

St. Louis Children's Hospital, the only pediatric hospital in Missouri named in the report, has appeared on the U.S. News Honor Roll nine times. The Children's Discovery Institute, a research collaboration with the School of Medicine, was launched earlier this year.

Both Barnes-Jewish Hospital and St. Louis Children's Hospital are part of St. Louis-based BJC HealthCare, the area's largest employer with more than 21,000 employees.

Virgin named department head, Unanue becomes Lacy professor

Herbert W. "Skip" Virgin, MD, PhD, has been named head of the Department of Pathology and Immunology, succeeding Emil R. Unanue, MD, who served in the position for 21 years.

As the new department head, Virgin becomes the Edward Mallinckrodt Professor of Pathology and Immunology.

The department is widely recognized for pioneering work in immunobiology, the study of how basic genetic and molecular mechanisms in the immune system defend against invaders and malfunction in autoimmune conditions such as multiple sclerosis and rheumatoid arthritis.

Virgin's goals include promoting departmental efforts to harness genetic information as a diagnostic tool, a core component of the university's BioMed 21 initiative.

His own research includes studies of how the immune system responds to chronic viral infections. In 2004, Virgin's group became the first to successfully grow noroviruses in the laboratory. Norovirus disease is characterized by frequent vomiting and diarrhea over the course of one to two days. The accomplishment is helping scientists seek ways to weaken norovirus for use as a vaccine.

Unanue has been named the Paul and Ellen Lacy Professor of Pathology. The chair is named for Unanue's predecessor as department head, Paul Lacy, MD, PhD, and his wife, Ellen.

"I am very honored to receive the Lacy chair, because Paul was not only a close personal friend but also someone whom I admired greatly," Unanue says. "He had a very significant influence in making the department a major center for biomedical research prior to my arrival here."

Unanue is internationally recognized as a leader in understanding how the immune system identifies foreign material, known to scientists as antigen, and how immune system T cells respond to it. The cells are important components of the body's response to infectious diseases; when misdirected against the body's own tissues, they also can make major contributions to autoimmune conditions including diabetes and arthritis. Through his continuing investigations of how immune recognition and attacks take place, Unanue has helped scientists gain important insights that may one day be harnessed to improve the body's defenses against diseases and to disarm mis-directed immune attacks.
Tumor wizardry wards off immune system attacks

Like the fictional wizard Harry Potter, some cancerous tumors seem capable of wrapping themselves in an invisibility cloak.

Researchers at the School of Medicine have found that pancreatic tumors hide from the body's immune surveillance by surrounding themselves with cells that make it hard for the immune system to detect them.

The tumor-protecting cells are white blood cells called regulatory T cells, or T-reg. Under ordinary circumstances, T-reg cells inhibit immune components responsible for killing unwanted cells. This allows T-reg cells to help prevent autoimmune reactions.

The scientists discovered that cancerous cells take advantage of T-reg cells' suppressor ability, enlisting them to keep the immune system at bay. Their report appeared in the July/August issue of the Journal of Immunotherapy.

"Earlier, we found that T-reg cells are much more prevalent in patients with breast cancer and pancreatic cancer than in healthy patients," says David C. Linehan, MD, associate professor of surgery and a Siteman Cancer Center researcher. "The new findings show that tumors are directly responsible for the increase of T-reg cells and can attract T-reg cells to their vicinity."

Linehan believes this could explain the failure of many experimental anti-cancer vaccines, designed to rev up the immune response to cancer cells. A tumor shielded with T-reg could circumvent an attack.

In mice implanted with pancreatic cancer, the researchers demonstrated that tumor growth caused an increase in T-reg cells in both the blood stream and in lymph nodes leading from the tumors.

When researchers blocked a signaling molecule (TGF-beta) that pancreatic tumors secrete, T-reg cells were no longer present in the tumor-draining lymph nodes, suggesting that TGF-beta has an important role in the tumor's cloak of invisibility.

Such information could lead to a method for blocking tumors from using T-reg cells for protection. Other research by Linehan and colleagues showed that in mice with pancreatic cancer, simply depleting T-reg cells slowed tumor growth and increased survival time.
Medical school, hospital unite to reduce hospital-acquired infections

Infectious disease experts at Washington University School of Medicine and Barnes-Jewish Hospital will participate in a new multicenter research network dedicated to assessing, treating and preventing hospital-acquired infections.

"As improved health care has led to extended life spans, the population of older patients who are more susceptible to hospital-acquired infections has increased," says Victoria J. Fraser, MD, the J. William Campbell Professor of Medicine and co-director of the division of infectious diseases. "Other growing patient populations that are vulnerable include those with suppressed immune systems and surgical patients."

The Centers for Disease Control estimates that each year about 2 million infections are acquired in health care settings, resulting in about 90,000 deaths and more than $4.5 billion in excess costs.

To support innovative research dedicated to stopping these infections, the Centers for Disease Control has announced $10 million in funding through its Prevention Epicenter program. Washington University and Barnes-Jewish Hospital will receive $300,000 annually for five years. In addition to faculty from the division of infectious diseases, researchers from the departments of medicine, surgery and pediatrics will contribute to the research.

A primary goal of the new effort will be to standardize reporting of hospital-acquired infections and antibiotic-resistant strains of pathogens.

Digital records boost quality of care, reduce errors and improve efficiency

Surgeons and staff no longer play the "Where's-the-chart?" game in the Division of Card thoracic Surgery at the School of Medicine. That activity recently became obsolete when the division switched from using paper files to a fully electronic medical record system.

"In our division, there might be six people vying for a patient’s chart," says Laura Ochoa, advance practice nurse in thoracic surgery. "The surgeon's assistant might have the chart so she can include dictation from the surgeon, I might need it to organize some tests, our research group might want it to see if the patient is eligible for clinical studies."

With the secure electronic system, authorized personnel can look at one chart simultaneously from individual offices — on the medical campus or at other clinical locations.

"The potential advantages for general thoracic surgery are huge, because we see a large number of new patients every week," says G. Alexander Patterson, MD, the Evarts A. Graham Professor of Surgery and chief of the Division of Cardiothoracic Surgery. "Most of those new patients require a significant number of investigations before we can make a plan for treatment, so it's an incredible amount of data to manage. The electronic format has really helped."

Electronic medical records also may improve patients' experiences. Pharmacy requests can be made with the push of a button, lab results and X-rays can be received by the system, and visits to multiple specialists are simplified because each physician has access to the same chart, complete with up-to-date allergy and medication information.
Riew and Yamaguchi receive Simon, Fox endowed professorships

Orthopaedic surgeons K. Daniel Riew, MD, and Ken Yamaguchi, MD, have been named to professorships at the School of Medicine. Riew is the Mildred B. Simon Distinguished Professor, and Yamaguchi is the Sam and Marilyn Fox Distinguished Professor of Orthopaedic Surgery.

"The School of Medicine is very grateful for the generosity of Sam and Marilyn Fox and of Mildred Simon, and these distinguished professorships are indicative of their commitment to our institution," says Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the School of Medicine. "These gifts not only will help support the great work being done by Drs. Riew and Yamaguchi, they also will help ensure the continued growth and success of our Department of Orthopaedic Surgery."

The Sam and Marilyn Fox Distinguished Professorship was created this year by the Foxes. The Simon Distinguished Professorship was established in 1998 through a bequest from Mildred B. Simon.

Richard H. Gelberman, MD, head of orthopaedic surgery and the Fred C. Reynolds Professor of Orthopaedic Surgery, says endowments such as these are vital to the School of Medicine's goal of recruiting and keeping top-quality researchers and clinicians.

Riew is co-director of the Spinal Research Fellowship, chief of Cervical Spine Surgery and director of the Orthopaedic Cervical Spine Institute. Yamaguchi, elected earlier this year to the board of directors of the American Academy of Orthopaedic Surgeons, is chief of the Shoulder and Elbow Service.

OTOLARYNGOLOGY

Cochlear implants: early use leads to better speech

"Bye-bye, bye-bye," said one 3 1/2-year-old child playing with a toy train, nine months after a cochlear implant partially restored his hearing.

In contrast, another child of the same age, implanted with a cochlear device nearly three years earlier, made a more sophisticated statement: "OK, the train's coming to get the animals and the people."

This testing session was part of research that indicates the earlier a deaf infant or toddler receives a cochlear implant partially restored his hearing.

The researchers tested spoken language skills of 76 children, all 3 1/2-years-old. They found that with increased implant time, the children's vocabularies were richer, their sentences longer and more complex, and their use of irregular words more frequent.

Nicholas notes that many of the children who received cochlear implants at the youngest ages have nearly the same spoken language skills as children with normal hearing.

"Kids with residual hearing can get some help from hearing aids, but cochlear implants give a tremendous hearing advantage over hearing aids; the implants provide more sound information," Nicholas says. "For example, high-frequency sounds are magnified more with cochlear implants, so kids can hear 's' sounds and 'ed' endings better. So they tend to catch on to plurals and verb tenses faster."

Although studies like this and others favor early implantation, the decision for or against cochlear implantation is frequently put off, Nicholas says. Hearing parents often find they need time to learn about deafness and potential treatments.

"Studies like ours are meant to help answer parents' questions about cochlear implants," Nicholas says. "Our overall goal is to focus on the best age for implantation. If the window of time for the best outcome is small, we want parents to know that."

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Damaged auditory hair cells cause hearing loss. Other vertebrates can regenerate the hairs. Could humans?

**BY STEVE KOHLER**

**F I T W E R E R E A S O N A B L E** to name the body's most valuable cells, the sensory receptors in the ear — the hair cells that translate sound pressure into electric signals that the brain can interpret — would be good candidates for the top 10 list:

- They total about 16,000 per ear, so there are none to spare. By contrast, each eye has 130 million photoreceptors.
- They're subject to damage by noise, the side effects of certain antibiotics, infection and, inevitably, aging.
- When they are lost, profound deafness is the result. And they don't grow back.

At least they don't regenerate in mammals. In other vertebrates, damaged hair cells in the inner ear regrow in an accelerated process that's otherwise almost identical to the one by which they were originally created during embryonic development.

The difference in regenerative ability drives the research of Mark E. Warchol, PhD, a research associate professor of otolaryngology working at Central Institute for the Deaf at Washington University School of Medicine, and Michael Lovett, PhD, professor of genetics. The two collaborate to understand what changes take place to shut down mammals' ability to regenerate hair cells.

A microscopic substance designed to affect tissue development is implanted into the ear of a chick embryo, above and right. The specimen will be incubated for three to 10 days, then studied for its effects.
Why is there this difference; what makes mammals the exception?” Warchol asks. “The regenerative mechanism is present in other vertebrates, and the cells are so similar.”

Warchol believes that an inhibitor is at work in mammals, and the goal is to understand the mechanism with an eye toward re-evoking the process of hair cell regeneration. The death of hair cells is “the bottom line of deafness,” and the “holy grail” is to improve or even cure hearing loss by regrowing them, Lovett says. The work is representative of the university’s BioMed 21 initiative, designed to bring together collaborators to speed clinical solutions from research discoveries.

Working with hair cells and the cells that support them from chicks, the researchers see regeneration begin 12 to 16 hours after injury. The process starts when supporting cells revert to a state that resembles a stem cell. Then, “the genetic regulatory pathways are re-activated, and new hair cells differentiate. They look mature and are functional within 10 days,” Warchol says. The process also appears to stop as it should, again mimicking embryonic development.

It takes about another 20 days to make final connections between hair cells and the brain, as chemical signaling molecules guide nerves to their targets. For example, the neuron responsible for delivering a 1-kHz signal has to connect to the 1-kHz-specific spot on the cochlea and, at the other end, to the 1-kHz-region of the brain. But by the time four weeks has passed, a completely deaf chick will again be hearing the infernal peeping of his or her clutch-mates.

Work done elsewhere shows that it may be possible to elicit the same reversal in lower mammals and, the hope is, ultimately in humans. Yehoash Raphael at the University of Michigan has introduced a virus that carries a critical gene for hair-cell development into the inner ears of deaf guinea pigs. New cells grow, Warchol says, and they look much like hair cells, though the full extent of recovery is not yet clear and awaits further study. “But that’s a profound effect, nonetheless” he says.

The Warchol/Lovett approach is different. Having first developed methods for maintaining sensory cells in vitro, they employ gene array technology to identify genes that are either activated or inhibited shortly after cell damage or cell death. By developing their own gene chips, they control costs and can perform large numbers of comparisons. They study sensory cells from both the chick’s ear and vestibular organ.

To simulate both cell death and the trauma of loud noise, the investigators apply a toxic antibiotic to kill or a laser to damage the two subsets of cells. Working in vitro, they precisely control timing, examining the cells at critical points. Recording changes in genetic activity from each of the four scenarios, they then create a Venn diagram of the
About 20 genes are always perturbed, and "those are likely to be the important players," Warchol says. Then, a powerful genetic manipulation technique that selectively knocks down an individual gene's protein product for a period of two to three days allows the researchers to rerun the experimental protocol and observe results. "We'd like to identify those genes that act as suppressors of the regeneration process," Warchol says, "and temporarily knock them down." But the process is tedious: the research began with 1,700 candidate transcription factor genes that act as switches, and the network of protein interaction is complex. The tough question is: "If we bring down one factor, how does that change reverberate through the network of activation?" Warchol says.

Next, they plan similar investigations in the mouse to observe which genes in that mammal are inhibiting regeneration and how they are interacting. "We'll overlay results from the mouse experiments on the chick data to compare and contrast genetic activity," Lovett says. If they can find transcription-factor genes specific to the mammalian ear, the potential exists to remove the innate inhibition to regeneration. "If we can suppress the suppressor, it may be possible to allow the natural regeneration of hair cells," Warchol says.

The day on which that is possible in humans may be far off, but the promise to reinstate what seems otherwise to be a lost capability could help those whose hearing has been damaged or eradicated by an increasingly noisy world, trauma or the aging that eventually affects everyone. The research reported here is funded in large part by the National Organization for Hearing Research Foundation and the National Institutes of Health.

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One way to discern the effect of a gene and the protein it expresses is to turn it off and observe the process in which you're interested, noting any changes. Medical scientists have devised a powerful process that uses the cell's own defenses to switch off individual genes.

Called small interfering RNA, the technique introduces into a cell a fragment of double-stranded RNA from the gene-of-interest's instruction for protein building. All cells have defenses against double-stranded RNA, because it usually is encountered only when a virus is present. As the cell's immune defense chops up what it believes is an invader, it also eliminates the similar protein product of its own genes. The result: expression of a single protein is suppressed. The effect lasts a few days, long enough to explore the effects, and appears to leave no side effects. "By using the normal cellular mechanism, there's no longer a need to genetically engineer an entire organism and grow it," says Michael Lovett.
Origins of Alzheimer's

Measuring A-Beta could lead to ways to abate it—and the onset of Alzheimer's. By Michael Purdy

Researchers have known since the early 20th century that a characteristic sign of Alzheimer's disease is that it leaves sufferers' brains riddled with plaques. The key ingredient of the plaques is a fragment of a protein known as amyloid precursor protein (APP). The fragment itself is called amyloid beta (Aβ).

The causes of excessive Aβ are often maddeningly elusive. That's partially because a wealth of environmental and genetic factors probably contribute to risk. But another significant question also obscures scientists' view of Alzheimer's origins: Do patients' brains make more Aβ, or are they unable to clear it out quickly enough?

A new test developed by researchers at the Alzheimer's Disease Research Center (ADRC) at Washington University in St. Louis may finally help resolve this mystery.

The test is the first to allow researchers to safely monitor production and clearance rates of Aβ in humans. In addition to helping scientists learn more about the origins of Alzheimer's disease, the test may help them improve its diagnosis and treatment.
Healthy bodies maintain a balanced rate of production and clearance of Aβ, a protein fragment that harms the brains of Alzheimer's patients. In Alzheimer's, Aβ must either be made in greater quantities or removed less efficiently. The test was devised to measure the rate of this process in order to provide data for better understanding the mechanics of Alzheimer's. The fast rate of change over a few days came as a surprise. To the researchers' knowledge, this experiment represents the first estimate of the synthesis and clearance rate of a protein produced in the human central nervous system.

It's very important to understand if patients have a decreased clearance rate or an increased production rate," says Randall J. Bateman, MD, assistant professor of neurology and lead developer of the new test. "If we find that it's mainly a problem in production or in clearance, then that's obviously what we want to be targeting with therapeutics."

Practically speaking, one of the biggest obstacles to understanding Alzheimer's disease has always been the delicacy and inaccessibility of the living human brain. Neuroscientists generally aren't too eager to directly poke or prod it. Researchers had found ways to measure Aβ levels in the brain by taking samples of cerebrospinal fluid. But like many other proteins, APP, the precursor to Aβ, is regularly produced, used, discarded and reproduced, starting the cycle again. This made a reading of a patient's Aβ levels like taking a photograph of a sink flooding with water: It was useful to know that the sink was flooding, but they still couldn't tell if the faucets had been opened wider or the drain was clogging.

The secret of the new test's success lies in a technique for temporarily tweaking brain chemistry that's so subtle it can only be detected by scientific equipment, not by brain cells or the chemical reactions that take place in the brain. In effect, it's a way of gently poking the brain without breaking anything.

"The vast majority of the carbon atoms in our body are what we call carbon 12, meaning they have 12 protons and neutrons in their nucleus," Bateman explains. "We give patients an intravenous infusion of the amino acid leucine, a building block for proteins, that has been labeled with carbon 13, which has 13 protons and neutrons in its nucleus."

The label is safe and non-toxic; rats have been raised entirely on food containing carbon 13, Bateman notes. All cells incorporate the labeled leucine into the proteins they make over the next several hours, including brain cells making APP.

Scientists take periodic samples of the subjects' cerebrospinal fluid through a lumbar catheter, purify the Aβ from the samples and then use a mass spectrometer to determine how much of the Aβ includes carbon-13-labeled leucine. By tracking how fast the percentage of labeled Aβ goes up, they can determine the Aβ production rate.

Bateman notes that the labeled leucine is very hard to separate out. "It behaves for all intents and purposes like the real thing, but that's why we chose it — because it doesn't interfere with the underlying physiology," he explains.
After the labeled Aβ level peaks, researchers stop infusing the label but continue to regularly sample the cerebrospinal fluid. As old, labeled Aβ is cleared away and cells no longer have the labeled leucine to incorporate into new Aβ, the percentage of labeled Aβ goes down, revealing its clearance rate.

Bateman developed the mass spectometry technique with extensive guidance and assistance from Kevin E. Yarasheski, PhD, associate professor of medicine and assistant director of the Washington University Biomedical Mass Spectrometry Resource, and staff scientist Ling Munsell, M.S. Yarasheski previously used a similar approach to measure production and clearance rates of muscle proteins.

Working in the laboratory of David M. Holtzman, MD, the Andrew B. and Gretchen P. Jones Professor and head of the Department of Neurology and with the support and guidance of John C. Morris, MD, the Harvey A. and Dorismae Hacker Friedman Distinguished Professor of Neurology and director of the ADRC, Bateman tried out the new test on six healthy, young volunteers.

Because Alzheimer's symptoms take many years to develop, some researchers had assumed that the creation and clearance rates for Aβ were very slow. But the initial test of the new technique suggested the opposite.

"Amyloid beta has the second-fastest production and clearance rate of any protein whose production rate has been measured so far," Bateman says. "In a time span of about six or seven hours, you make half the amyloid beta found in your central nervous system."

As expected, in the first six healthy volunteers, the clearance rate closely matched the production rate.

"Without a balance in those two rates, a person will end up with increasing or decreasing amounts of amyloid beta in the brain," Bateman notes.

Bateman and his colleagues have begun applying the test to Alzheimer's patients to determine whether their production or clearance of Aβ is changing. There's also substantial potential to apply the new test in clinical contexts.

Previously, the only way to assess the effectiveness of a new Alzheimer's drug was to follow the mental performance of patients receiving the treatment over many months to years.

"This new test could let us directly monitor patients in clinical trials to see if the drug is really doing what we want it to do in terms of Aβ metabolism," Bateman says. "If further study confirms the validity of our test, it could be very valuable for determining which drugs go forward in clinical trials and at what doses."

The test also may be useful in diagnosis of Alzheimer's prior to the onset of clinical symptoms, which occurs only after Alzheimer's has inflicted widespread and largely irreversible damage on the brain.

"One of the problems with Alzheimer's disease and most dementias is that once they set in, even if you stop the offending process, the brain doesn't necessarily reverse and heal itself to its normal state," Bateman explains. "We may be able to use a modified version of this new test to detect a metabolic imbalance in amyloid beta before people become demented, and start treatment then."

The technique may have applications beyond Alzheimer's disease. Other research groups have expressed interest in applying the new test to neurological disorders such as Huntington's disease, Parkinson's disease and prion protein diseases.

The secret of the new test's success lies in a technique for temporarily tweaking brain chemistry that's so subtle it can only be detected by scientific equipment, not by brain cells or the chemical reactions that take place in the brain.

Aβ from human cerebrospinal fluid has been processed for measurement of the label by a sensitive device called a mass spectrometer, which can weigh the difference of a single neutron (smaller than an atom).
No bones about it

Calcium is a very good thing — in the right places. Bones contain most of the body's calcium, providing the body with a sturdy frame; the rest forms the teeth. But when calcium gets into blood vessels, the resultant hardening can threaten people's health.

Dwight A. Towler, MD, PhD, director of the Division of Bone and Mineral Diseases, says that in some people, blood vessels and valves can become the second-most calcified structures in the body.

Until recently, scientists and physicians knew very little about how calcium was deposited in blood vessels or how to get rid of it.

Within one X-ray, two diseases of calcium metabolism are pictured: The hip has fractured due to lack of calcium (upper arrow), while the mineral's buildup in the femoral artery has hampered circulation in the leg (lower arrow).
Calcification of vascular components often develops with age and with disorders such as elevated cholesterol, high blood pressure, diabetes and kidney disease. While many of us are familiar with calcification of atherosclerotic plaques, those nasty lumps that can block arteries and contribute to clot formation, less well known is another common type of arterial calcification: medial artery calcification, or MAC.

MAC describes calcium deposition within the matrix of artery walls and encircling the entire vessel. The hardening of the arteries associated with MAC interferes with the normal flexibility of blood vessels, which in turn impedes the proper flow of blood to tissues and puts extra stress on the heart.

"Clinical data from populations susceptible to type 2 diabetes have shown that MAC is the single best predictor of risk for lower leg amputation and for mortality," says Towler, the Ira M. Lang Chair in Medicine and professor of molecular biology and pharmacology. "But I'm just old enough to remember being told that MAC isn't medically relevant because it doesn't block the artery like plaques can."

Towler says MAC is largely unaddressed by available clinical treatments, even though the problem is widespread and serious. "I recently consulted on a patient with kidney failure whose blood pressure falls precipitously when she stands. In her X-rays, vessels appear with calcification all along them — you shouldn't be able to see blood vessels in X-rays at all. Because hers are calcified, they can't contract to compensate for the change in posture when she stands. The treatment options for such a patient are limited."

Like many patients with arterial calcification, this woman also has osteoporosis. Physicians have noted that bone calcification and blood vessel calcification are often linked in a reciprocal relationship — as one goes down, the other comes up. This connection hints at something more complex in arterial calcification than previously realized.

Earlier thinking held that calcification of arteries is a passive process; that is, calcium settles in blood vessel walls or deposits at places where cell death occurs. But Towler and colleagues have uncovered processes that actively create calcium deposits in arteries.

One of the first discoveries on the way to this new understanding of vascular calcification was the finding that calcifying atherosclerotic plaques produced a powerful substance known to be involved in the repair of bone — bone morphogenetic protein-2 or BMP2. A growth factor, BMP2 was first identified at sites of bone formation and has since been successfully used to speed healing of broken bones. BMP2 promotes vascular calcification by activating Msx2-Wnt signaling, a bone-forming mechanism critical for skull and tooth calcification during embryonic development.

A few years ago, Towler and colleagues performed experiments that marked another turning point in thinking about vascular calcification. They gave parathyroid hormone to laboratory mice to see how it would affect their arteries. Ordinarily, pulses of parathyroid hormone increase bone mass and bone strength; it currently is being used as a treatment for osteoporosis. To Towler's surprise, instead of increasing calcification in blood vessels of the mice, the hormone inhibited the vascular Msx2-Wnt signals that promoted arterial calcification — exactly the opposite of what occurred in bone.
Calcium can build up in the wrong places within the body. Calcium, an essential building block of the human body's skeleton, travels throughout the bloodstream. It can, however, deposit in blood vessels, mineralizing to form bone-like tissue, thwarting the smooth flow of blood to organs. Understanding how and why this happens to people with diseases such as diabetes, kidney failure and high cholesterol may lead researchers to find ways to keep calcium stored only where it is needed.

BY ERIC YOUNG  RESEARCH IMAGES AND DATA: TOWLER LAB

Lost flexibility of vessels strains the heart: medial artery calcification

Calcium deposits encircle and stiffen an otherwise naturally elastic artery. The heart must work harder to circulate blood with no kinetic assist from the rubbery rebound action of a healthy vessel. This condition is a corollary of diabetes and end-stage renal disease.

In addition to nutrients, capillaries can pipe trouble within the walls of the artery, including blood fats that create adipocyte cells and recruit tissue macrophages. Together, these secrete inflammatory signaling hormones, which ultimately generate vascular bone-forming cells — derived from certain smooth muscle cells — that direct calcium deposition.

Circulation in the soft tissue in this foot will be impaired as the dorsalis pedis artery calcifies. Such a damaged vessel's calcium-rich tissue is highlighted in red (below).
Vessel blockage creates a coronary time bomb: atherosclerotic (fibrous) calcification

Deposits of lipid, protein, smooth muscle cells and calcium deform the vessel on one or more sides. These buildups are characteristic of high cholesterol. In addition to stiffening the vessels, this process creates an abnormal surface that can trigger arterial blood clots.

High cholesterol in the blood builds up beneath the inner lining of the artery. Inflammation, cell death and fibrosis initiate calcification. This vascular “scar tissue” induces the formation of bone and cartilage cells — derived from certain smooth muscle cells — that direct further calcium deposition.

Calcium collects in the lining of the aorta deep within the body. This not only stiffens vessels but predisposes them to arterial blood clots.

Atherosclerotic calcification is widely known but unfortunately not always clearly distinguished from medial artery calcification.
"Pulsatile parathyroid hormone signaling turns out to be an exquisitely smart hormonal rhythm," Towler says. "It directs the deposition of calcium in bones while simultaneously protecting blood vessels from calcification. We need to find out what mechanisms could account for that."

The researchers found that blood vessels with MAC have gene activities commonly seen in bone and tooth formation. As Towler points out, if gene programs are turned on during calcification, that shows the process is definitely not passive.

The reason patients can have osteoporosis along with artery calcification - why bones lose calcium as arteries gain it — lies in the fact that some cells in blood vessel walls can be molecularly "re-programmed" to become bone-making cells. These cells react in an opposite way from bone-making cells in the skeleton in response to the metabolic, hormonal and inflammatory changes that occur with diabetes, renal failure and advanced age.

Investigations that followed these discoveries mapped out a detailed system of molecular signals involved in vascular calcification. Spurred on by high fat diets or diabetes, for example, cells in the outer layer of arteries begin producing BMP2. Reactive oxygen molecules and inflammatory substances produced by macrophages and fat cells play a role in initiating this step.

Tiny blood vessels, or capillaries, within the walls of large arteries carry signal substances generated in reaction to BMP2. These signals combine to initiate a series of responses that transform arterial cells into bone-forming cells. The transformed cells use calcium to create an inflexible, brittle core within the vessel walls. A similar process leads to calcification of atherosclerotic plaques, but with the added contributions of cell death.

"Physicians don't generally approach vascular medicine this way," Towler says. "They tend to think of what's happening in the layer of cells that lines the interior of vessels, where the blood flows. But we've found that it's the outer layer, the one furthest from the blood flow, where the important reactions are taking place that lead to calcification of the type seen in diabetes and kidney disease."

This information about vascular calcification lends hope for effective treatments. It says that vessels aren't just absorbing calcium and turning to stone. Instead, the calcified areas of MAC are — like bone — living tissues undergoing active remodeling and repair. And that means the process could potentially be reversed — at least for this one type of vascular calcification.

"If medial artery calcification is a disorder that responds to 'osteotropic' or bone formation hormones, such as parathyroid hormone, then it should be therapeutically tractable," Towler says. "If we take some of the things that we know about mineral deposition in the skull and long bone and begin to study those pathways in the vasculature, we may be able to inhibit it. That's an entirely new way of thinking about the problem."
Carpal tunnel syndrome gets all the press.
A lesser-known nerve affliction is more down to earth.

BACK ON YOUR FEET AGAIN

BY BETH MILLER
this spring, Adam Tinnin, a normally healthy, active 16-year-old, experienced a viral infection that caused mouth sores, hives, then tingling and numbness in his feet. In a matter of days, he had no feeling in his feet and couldn't walk.

Adam went to the emergency room twice near his home in Sikeston MO, where doctors diagnosed a virus and sent him home with medication to treat the hives. When he lost the feeling in his feet, he and his mother, Stephanie, came to Washington University Medical Center to see specialists about his condition. He spent three weeks as an inpatient at St. Louis Children’s Hospital undergoing dozens of tests, including nerve biopsies, a spinal tap and diabetes testing, which all were normal. Adam, frustrated and distressed, was preparing for discharge, worried that he might spend the rest of his life in a wheelchair.
"I felt like giving up," Adam says. "I would lie in my bed and cry and pray that someone would come along and figure out what was wrong. I felt that all hope was gone."

Susan E. Mackinnon, MD, the Sydney M. Jr. and Robert H. Shoenberg Professor of Surgery and chief of the Division of Plastic and Reconstructive Surgery, happened to be having lunch in the doctor's lounge at the hospital on a day when Adam's case was being discussed. Mackinnon's interest was piqued, and she asked if she could examine Adam.

After the examination, Mackinnon was confident she knew what Adam's trouble was — a neuropathy with tarsal tunnel syndrome, similar to carpal tunnel syndrome, but in the ankles.

To diagnose tarsal tunnel syndrome, also called posterior tibial neuralgia, Mackinnon uses a test she developed with a colleague that she calls the "scratch-collapse" test. Adam's test was positive for irritation of his tibial nerve at the tarsal tunnels.

"I scratched along the tibial nerve and his arms collapsed, indicating a problem with that nerve," Mackinnon says.

Tarsal tunnel syndrome, which can be difficult to diagnose, is caused by pressure on the tibial nerve, which follows a long route down the back of the leg to the ankle, where it turns and curls below the inside of the ankle. Sometimes ligaments and other tissues that surround the nerve press on it, causing pain, a burning sensation and tingling on the sole of the foot. In Adam's case, it also caused paralysis and prevented him from walking.

Mackinnon says she believes a prior ankle sprain made him susceptible to the development of this acute tarsal tunnel.

"While tarsal tunnel syndrome is not a rare condition, it is very uncommon that it becomes so severe that a patient can't walk, especially in someone so young," she says.

Mackinnon performed tarsal tunnel release surgery on Adam's left foot this past May. During the one-hour procedure, she cut the covering over the tibial nerve to relieve the pressure.

By late June, he had feeling back in his toes and could walk without assistance. About a month after the second surgery, he returned to his job at UPS and was back to being a normal, healthy teenager.

Adam, who is just starting his junior year of high school, plans to use the experience to fuel his drive to become a physician, with strong leanings toward anesthesiology or plastic surgery. He also would like to attend Washington University as an undergraduate in two years.

"I took for granted what I had before, but when everything was swept out from underneath me, I knew then that anything can be taken away from us," Adam says.

The son of a pastor and the oldest of five children, Adam says the experience has changed him for the better and made him a more spiritual person.

"Now when I see people in wheelchairs, in my spirit I begin praying for them because I know how it is and what it's like to be there," he says.

And Adam says he is very grateful to Mackinnon for taking the time to care and for changing his life.

"I believe Dr. Mackinnon was sent by God into my room that day, and I know I will never forget her."

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Outlook 23
Celebrating scientific accomplishments that history almost forgot

In Doctor Franklin's Medicine, Finger presents a colorful and context-rich analysis of Franklin's medical efforts. More than a simple listing of Franklin's medical contributions, Finger's book reveals what was theorized about health and disease early in the 18th century and shows how Franklin strove to improve medicine with careful observations, actual experiments and hard data.

"Franklin was a rare bird," Finger says. "His broad contributions are especially remarkable in that he had no medical training and, in fact, only two years of classroom education. What is even more amazing is that he came from the colonies, where life was still a struggle — not from a major European cultural center."

One of the unique features of Finger's book is that he shows how Franklin's life and medical

"What distinguished Franklin ... was that he approached clinical medicine with the mindset of an experimental natural philosopher," says Stanley Finger, PhD, at an exhibit of the experimental electrical apparatus of Franklin's day.
views were partly shaped by personal events, including the loss of his son, Francis, to smallpox, and his own visual problems, painful gout and massive bladder stone.

A lack of formal medical training was no barrier to practicing medicine in 18th-century America. In fact, only a small percentage of colonial healers had formal medical training, and even fewer possessed college degrees.

"What distinguished Franklin from the myriad other colonials who practiced or dabbled in medicine was that he approached clinical medicine with the mindset of an experimental natural philosopher," Finger writes. "He skillfully designed experiments, collected data and compiled tables to determine trends and outcomes. He also read voraciously, contacted authorities to solicit their opinions and searched for historical antecedents. Moreover, Franklin had a remarkable ability to recognize the good ideas of others and the tenacity to move these ideas toward a productive end."

Some of Franklin's contributions to medical theory and practice

- **Medical institutions** Instrumental in founding the first major civilian charity hospital and the first medical school in the colonies.
- **Smallpox** Studied inoculation as a weapon against epidemics of smallpox, becoming one of the first to use statistics in a public health campaign.
- **Common cold** Investigated causes of the cold, concluding that people spread colds, and that they probably have something to do with the transmission of microscopic particles.
- **Medical inventions** Bifocal lenses and a "long arm" that extended the user's reach were among his many inventions aimed at making life easier for the aged and afflicted. He also was involved with designing and making what might have been the first flexible urinary catheter in the colonies.
- **Lead poisoning** Observed that many patients suffering from stomach pains and other symptoms were craftsmen in trades exposed to high levels of lead. He helped colleagues understand the perils of lead-contaminated rum and other beverages, and warned of lead in household implements, such as pans and milk storage containers.
- **Medical electricity** Experimented with the use of electrical shocks to treat paralysis, blindness, deafness, hysteria and depression.
- **Exercise** Recommended daily swimming and stair climbing, surmising that health benefits were not necessarily linked to the length or type of exercise, but hinged instead on the degree of body warmth generated — now referred to as regular cardiovascular exercise.
- **Quackery** Used experiments to debunk the claims of Franz Mesmer, who believed he could cure people by harnessing and directing an invisible magnetic force that permeated the cosmos.
Taking the plunge
Two alumni who just can’t keep their feet on the ground

Lance A. Roy, MD 03, goes to great depths to understand how the human body reacts to life underwater.

He currently serves as a diving medical officer and biomedical researcher at the Navy Experimental Diving Unit in Panama City FL. Roy studies diving medicine, which explores breathing machines and decompression techniques, because it closely relates to his chosen medical specialty, anesthesiology.

As a diving medical officer, he is developing new techniques that help people avoid the “bends,” decompression sickness that occurs when a diver surfaces too quickly. The bends results in nitrogen bubbles forming in the bloodstream and tissues of the body; in the most serious cases, the condition can lead to death.

As part of his research, Roy both conducts and participates in experimental research dives that go beyond the limits set by current U.S. Navy diving tables. Many of those dives take place in the Ocean Simulation Facility, a one-of-a-kind, 55,000-gallon hyperbaric facility that can support dives to 3,000 feet.

Roy considers serving in the U.S. Navy a privilege, but is constantly reminded of the personal sacrifices military physicians make. Many of his friends have spent months, or even years, serving in Iraq and Afghanistan. Sadly, a colleague at the Naval Medical Center San Diego was killed in action not long after the war in Iraq began. And Roy’s wife, Trina, a naval flight surgeon, is deploying soon to Iraq for a seven-month tour.

“The selflessness of the individuals in the military is inspiring and pushes me to work harder...”
Lance A. Roy, MD 03

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“The selflessness of the individuals in the military is inspiring and pushes me to work harder in search of new and safer diving techniques and technologies so that the frontline soldiers and sailors have the best possible chance for success,” he says.

After his stint with the diving unit, Roy plans to focus on anesthesiology. He has completed an internship at the Naval Medical Center San Diego and will begin a residency in anesthesiology in a year or two. He plans a career in academic medicine that will draw on his experiences conducting research for the Navy.

He and his wife share a home in Fort Walton Beach FL, with two cats and a yellow Labrador retriever puppy, Titan, that they’re training as a competitive agility dog. “Thus far, he’s a little lazy, but we hold out hope,” Roy says.

Lance A. Roy, MD 03, makes a SCUBA dive in the Testing and Evaluation Pool at the Navy Experimental Diving Unit (NEDU) in Panama City, Florida.
Ralph Glasser, MD 81, almost missed his medical school graduation.

An experienced skydiver, he planned to make a surprise jump into the ceremony, but unexpected high winds changed that.

He overshot the Quad, landing next to a car on a parking lot in downtown University City. Coincidentally, he knew the driver, Carl G. Harford, MD, his former mentor at the Veterans Hospital, who gave Glasser a ride to graduation with only minutes to spare.

"None of my classmates knew why I spent the day's festivities wearing shoes with holes torn in them," he says.

During medical school, Glasser had planned to become a surgeon. But a six-week preceptorship in anesthesiology during his fourth year and one month of anesthesiology during a general surgery residency at Michael Reese Hospital in Chicago changed his mind.

"Anesthesiology was the synthesis of everything I learned in medical school — critical care and applied pharmacology at its best," he says. "I also decided that all the surgeons were grumpy and all the anesthesiologists were happy. That spoke volumes to me."

In his fourth year of medical school, Glasser took flying lessons at Parks Bi-State Airport in Illinois. After more flight training during residency in Chicago, he flew a rented plane to his first job interviews. He now is an accomplished aerobatic pilot, performing with the Trojan Horsemen, a six-plane aerobatic team, at air shows across the country.

A partner in an anesthesiology practice in Springfield IL since 1984 and chairman of the anesthesiology department at Southern Illinois University School of Medicine in Springfield for more than a decade, Glasser says satisfaction comes easily in his job.

"There is something unique about every case, and there are innumerable techniques and nuances that enable us to approach each patient as an individual," he says. "Recognizing the needs of the patient and being able to provide comfort and reassurance to someone facing surgery is highly rewarding."

Glasser also enjoys spending time with Diane, his wife of 25 years, and his 16-year-old daughter, Sarah, who shares his passion for SCUBA diving, skiing, snowboarding, shooting sports and travel.
Leading the way
Couple sets standard for university involvement, giving

Marilyn and Sam Fox, BS 51, both grew up in Missouri homes with few luxuries. But when either family had extra pennies, they put them in a little blue box. Those boxes, distributed by the Jewish National Fund, collected money to be sent to Israel to fix roads and develop infrastructure.

“I always was taught that you shouldn’t just think of yourself, you should also do for other people,” Marilyn Fox says. “I also wanted to be a model for my children and help them understand there’s a bigger world out there.”

“I think everyone has an obligation to give back, of themselves or of their money,” Sam Fox says. “A community is only as good as the people who live in it.”

Sam Fox, BS 51, and Marilyn Fox.
In 1976, Sam Fox started Harbour Group Ltd., a privately held firm that acquires and builds businesses. Since then, the firm has bought more than 140 companies, and Fox, the chairman and chief executive officer, has become one of St. Louis' most prominent business and civic leaders.

Marilyn Fox also has taken an active role in many organizations, including the Missouri Botanical Garden, the Jewish Federation of St. Louis and the Variety Club. In 1992, she was elected the first female president of the Jewish Community Center in St. Louis and led a successful $17 million campaign for its satellite facility in Chesterfield MO.

This year, the Foxes established the Sam and Marilyn Fox Distinguished Professorship in Orthopaedic Surgery, held by Ken Yamaguchi, MD. "Dr. Yamaguchi is bright, dedicated and the kind of person you want to reward," says Sam, a patient of Yamaguchi's. "It's our honor to assist the school, the department and its head, Dr. Richard Gelberman."

Marilyn and Sam both have great admiration for Washington University and say they can't do enough to repay the school. Sam is a lifetime member of the university's Board of Trustees and served on the Board's executive committee. He also chaired the public phase of the Campaign for Washington University, which raised more than $1.5 billion.

"Washington University gave me the tools I needed at the time I needed them," Sam Fox says. "I can't imagine where I'd be today without those tools. I'm forever grateful."

Sam's father came to the United States in 1914 from the Ukraine with little more than a knapsack on his back. He eventually settled his family in the tiny town of Desloge MO. Sam's father was the consummate entrepreneur, his son says, trying his hand at everything from buying animal furs from farmers to manufacturing mattresses and eventually ending up in commercial real estate. "You can't sit around the kitchen table all your childhood with the likes of my father, with his tremendous enthusiasm for business, without catching the fever," he says with a laugh. "I caught the fever, or perhaps pneumonia."

Sam also was greatly influenced by his older sister, Esther, who strongly urged him to get a college education. He started saving for that education while still in high school by working long hours each summer in a Del Monte factory in Rochelle IL, canning corn and peas.

Growing up in Desloge during the Depression, Sam received very little exposure to the wider world. There was no television, there was no library, and the entire high school faculty was made up of four or five teachers. "When I attended Washington University, it was like a light bulb turning on," he says. "It brought the whole world in focus, and I couldn't get enough of it."

The only one of seven siblings to graduate from college, Sam earned his degree in business administration with honors. He sharpened his business skills working with his brother, Irwin, in a business that produced powdered iron for the chemical industry. After his brother became ill, they sold the business. Sam later founded Harbour Group.

Sam now divides his time between his business, his community, travel and his family. He and Marilyn have five children and 14 grandchildren.

Two of their children and some of their children's spouses have earned graduate degrees from Washington University, and one of their granddaughters earned her bachelor's degree at the university this past May.

Besides reveling in their family, the Foxes have taken great satisfaction in watching the university grow and change. "It's been exciting to watch Washington University become a leading institution," Sam Fox says. "We travel a lot, and we hear about Washington University all over the country and indeed the world."

"Washington University gave me the tools I needed at the time I needed them. I can't imagine where I'd be today without those tools. I'm forever grateful."

—SAM FOX, BS 51
Giving back through service

Sometimes even the familiar can take you by surprise.

For Jeffrey L. Thomasson, MD 82, the new president of the Washington University Medical Center Alumni Association, the School of Medicine was both the familiar — and the surprise.

Thomasson grew up in a St. Louis medical family, in which both of his parents were School of Medicine alumni, Mary Louise (MD 51) and Robert (MD 50) Thomasson, as was his uncle David Thomasson (MD 49). Even his godmother and close family friend Meredith Payne (MD 50) holds alumna status.

"I knew Washington University was a fine medical school, but I had no idea how fine it was," Thomasson says. "It wasn't until I got an outside perspective from people at other institutions that I learned I had grown up next to something wonderful."

Thomasson, a neuroradiologist, is president of West County Radiology Group and vice chairman of the Department of Radiology at St. John's Mercy Medical Center.

One mentoring relationship during his student days helped set him on the path to a radiology career. Louis A. Gilula, MD, professor of radiology, orthopaedic surgery and of plastic and reconstructive surgery at the School of Medicine, was Thomasson's faculty adviser, checking in on Thomasson and later interacting with him during a fourth-year radiology elective.

"Dr. Gilula is very unassuming, but an incredible radiologist," he says. When Thomasson began residency at Saint Louis University, a musculoskeletal radiologist there mentioned Gilula's reputation.

"I hadn't realized until then that he's a world-famous skeletal radiologist," Thomasson recalls. "I found out that he is one of a handful of world-renowned experts in the field."

Now approaching his 25th reunion, Thomasson finds his WUMC Alumni Association leadership role a way to repay a debt and connect with today's medical students.

"Serving as president will help me to give something back to the medical center," he says. "People can do that with teaching, contributions, or other alumni activities. I'm happy to be one person in a long succession of people to perform this role."

Today's students, he is quick to note, not only face the academic demands that have always been part of a medical education, they also face challenges of increased scrutiny by government and consumer agencies, more reliance on evidence-based medicine, and increasing concerns about how to finance health care for an aging population.

"The challenges for new physicians will be monumental," Thomasson says. "But I think people emerging from Washington University School of Medicine will be well prepared for basic and clinical science applications. They'll also have their own personalities, energy and interpersonal skills to be able to make the most humane use of that knowledge."
Students benefit from alumni funding

Medical students coached women through labor, staged a full-scale musical and taught middle school students about HIV/AIDS—all as a result of decisions made by the Washington University Medical Center Alumni Association during the past year.

Janet Mosley Ruzycki, MD 81, president of the Alumni Association’s Executive Council for 2005-06, reported the year’s accomplishments to alumni gathered in May for Reunion 2006.

More than $50,000 was designated to student-initiated projects in community service, science outreach and the arts. Groups including the Perinatal Project, the Forum for International Health and Tropical Medicine and the Student National Medical Association made successful funding requests and demonstrated the broad spectrum of involvement by this year’s medical students.

The Executive Council also designated funds to primary care preceptorships, which offer students a summertime opportunity to assist in providing primary care.

Scholarship funding of $160,000 from the Executive Council, combined with School of Medicine funds, provided full-tuition support to 16 Distinguished Alumni Scholars.

“We name each scholarship in honor of alumni who currently serve or formerly served on the school’s faculty,” said Ruzycki at the annual business meeting.

This year’s alumni selected for the honor are Elmer B. Brown Jr., MD 50, Lewis C. Fischbein, MD 74, Richard W. Hudgens, MD 56, and Bernard L. Shore, MD 77, all of whom will be paired up with students in the incoming first-year class.

In celebration of the Farrell Learning and Teaching Center’s first year of operation, the Executive Council allocated $60,000 for the facility and also funded social activities for the first- and second-year classes.

New officers and members who were elected at the Annual Business Meeting began their terms on July 1, 2006.
It’s another record year!

The School of Medicine closed the books on its 2005–2006 Annual Fund on June 30, 2006. Each year, the Annual Fund provides important and appreciated support for the School of Medicine, its students and its faculty. This year’s successful effort includes some notable new records, thanks to the generosity of our alumni and friends.

- Gifts to the School of Medicine's Annual Fund surpassed $3 million for the first time ever. More than 6,500 donors participated in setting this new record.
- The Eliot Society (Annual Fund donors of $1,000 or more) grew to 884 members, smashing the standing record of 818 members set two years ago.
- Health Administration alumni raised the bar for the third consecutive year, making $53,665 in gifts to support their program.

MD Reunion 2006
The eleven MD classes celebrating reunions from the 10th to the 60th last May played an important part in this successful Annual Fund. Reunion class gift efforts raised more than $350,000 in Annual Fund support; overall, 46 percent of these reunion alumni participated in giving. The total raised — including unrestricted and restricted support — was $784,139 in gifts and commitments.

Alumni Results by Program

<table>
<thead>
<tr>
<th>Program</th>
<th>Percent Participation</th>
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<tbody>
<tr>
<td>MD Alumni</td>
<td>32%</td>
</tr>
<tr>
<td>Physical Therapy</td>
<td>25%</td>
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<tr>
<td>Health Administration</td>
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<td>Nursing</td>
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<tr>
<td>Occupational Therapy</td>
<td>17%</td>
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<tr>
<td>Former House Staff</td>
<td>16%</td>
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The Class of 1981, led by gift chair Michele Kemp, MD 81, launched an Endowed Scholarship Fund in honor of its 25th reunion. The class joined together to raise $55,300 in gifts and commitments, surpassing the $50,000 goal to permanently endow their scholarship. This makes the Class of 1981 the 13th consecutive class to mark its 25th reunion by establishing a scholarship in the name of the class.

New alumni begin philanthropic careers

- The MD Class of 2006 left its mark on the School of Medicine by establishing the Class of 2006 Faculty Mentoring Award. More than 52 percent of the class made pledges and gifts to support the effort. The Washington University Medical Center Alumni Association lent its support by pledging to match gifts 2-to-1.
- The Class of 2006 in the Program in Physical Therapy set a record with its participation in the PT Young Alumni Gift, which supports a scholarship award each year. More than 66 percent of the class made a pledge — and it is only the fourth graduating class to support this effort!
classnotes

1940s

Lawrence W. O’Neal, MD 46

O’Neal is the chief editor of an English-language edition of Dr. Wu Yingkai’s Memoir: Seventy Years (1927–1997) of Studying, Practicing and Teaching Medicine. This edition of the autobiography is scheduled to be published in China by the end of the year. Wu trained in thoracic surgery at Barnes Hospital under Evarts Graham, MD, from September 1941 through July 1942. O’Neal first became interested in Wu’s story after arriving at Washington University School of Medicine as a medical student shortly after Wu’s departure.

Russell D. Shelden, MD 49

Shelden was presented the Distinguished Service Award for 2005 by the Missouri Society of Anesthesiologists for outstanding service in anesthesiology at the group’s April 2006 annual meeting in St. Louis.

1950s

Jack L. Titus, MD 52, PhD

Titus received the John J. Andujar Citation of Merit Award from the Texas Society of Pathologists in recognition of distinguished service and teaching excellence among pathologists. Several of his previous honors include the Distinguished Achievement Award of the Society for Cardiovascular Pathology (1993), the Harland J. Spjut Award for Distinguished Scholarly Achievement of the Houston Society of Clinical Pathologists (1993), and the Service to Humanity Award of the United Hospital Foundation (2004).

Robert C. Packman, LA 53, MD 56

Packman has joined the board of directors of the March of Dimes St. Louis division.

Adel A. Yunis, MD, HS 57

Yunis is the author of an autobiography titled Call Me Del: Dogged in the Pursuit of Excellence (trafford.com/05-0708) in which he recounts his life’s story beginning in Lebanon and his journey to the United States to study hematology with William J. Harrington, MD, and Carl V. Moore, LA 28, MD 32, at Washington University School of Medicine. His scientific achievements and disappointments, as well as some of his thoughts on what makes a medical school great.

Theodore H. Gaster II, MD 57

Gaster’s hobbies include bicycling, photography, traveling and keeping track of his grandkids. Since his retirement in 1997, he has served as a grade school science volunteer and educational foundation member.

Theodore J. Brickner Jr., MD 58

Brickner will receive the designation of Fellow of the American Society for Therapeutic Radiology and Oncology on November 5, 2006, at a special ceremony during the society’s 48th annual meeting.

1960s

Nicholas T. Kouchoukos, MD 61

Kouchoukos, a cardiothoracic and vascular surgeon, participated in a ribbon-cutting ceremony on May 11, 2006, commemorating the opening of the Kouchoukos Cardiac Education Center at Missouri Baptist Medical Center. The center was made possible through the generosity of Kouchoukos and his wife, Judy.

Christine L. Mackert, MD 62

Mackert, a retired anesthesiologist, enjoys traveling and climbing in many regions of the world. As leader of the Mazamas mountaineering organization, hers is only the second five-term presidency in the organization’s 112-year history. She lives in Portland OR.

David H. Hussey, MD 64

Hussey will be honored with the designation of Fellow of the American Society for Therapeutic Radiology and Oncology during the society’s 48th annual meeting in November 2006.

Peter W. Broido, MD 67

Broido enjoys contemporary art and serves as a volunteer at the Museum of Contemporary Photography in Chicago.

1970s

Jay Robert Harris, MD, HS 71

Harris will become a Fellow of the American Society for Therapeutic Radiology and Oncology at a special
ceremony during the society's 48th annual meeting in November 2006. He currently serves as professor of radiation oncology and chair of the Department of Radiation Oncology at Harvard Medical School.

Kerwin Jong Lee, MD 77
Lee enjoys creative writing, meditation, listening to jazz and serving meals to the poor with others from the Shattuck United Methodist Church in Berkeley CA.

Michael Bryant Kimmey, LA 75, MD 79
Kimmey was awarded the 2006 Rudolf V. Schindler Award by the American Society of Gastrointestinal Endoscopy (ASGE) and its foundation. The award highlights his accomplishments in endoscopic research, teaching and service to the ASGE.

1980s

Bharat B. Mittal, MD, HS 81
Mittal will receive the designation of Fellow of the American Society for Therapeutic Radiology and Oncology on November 5, 2006, at a special ceremony during the society's 48th annual meeting.

Michael Gruenthal, MD, PhD 81
Gruenthal was recently hired by the Albany Medical Center to chair its neurology department and serve as co-director of its Neuroscience Institute.

1990s

James Zanawar Lai, MD 92
Lai currently serves as president of Houston Eye Associates Foundation and practices pediatric ophthalmology at Houston Eye Associates. His wife, Jenny, practices physical medicine and rehabilitation. They have two children: Tommy, 3, and Emma, 1.

Candee Meadows Krueger, PT 92
Krueger and her husband, Todd, had a baby girl, Sophie Carolyne, on March 6, 2006. Sophie joins sister Mollie, 7, and brother Thomas, 2.

Jacquelyn Nieboer Fiss, OT 94
Fiss and her husband, Mike, welcomed their second child, James Alexander Fiss II, on April 2, 2006. Jacquelyn continues to work part-time consulting for the Colorado Foundation for Medical Care.

Karen E. Ruecker, MD 96
Ruecker is a pediatric hospitalist at St. John's Mercy Medical Center in St. Louis MO. She serves on the board of the Missouri chapter of Healing the Children, a national organization dedicated to providing various types of health care for children in need. Ruecker and her spouse, Adam C. Eaton, MD 97, MA 97, have two children.

Stephen A. Rector, HA 96
Rector is the new president and chief executive officer of Regional Medical Center Bayonet Point, the second-largest hospital in Pasco County FL.

IN MEMORY

Edward O. Damron, MD 39
Damron died on July 8, 2006, at the age of 92. After graduating from Washington University School of Medicine in 1939, he did his internships at Missouri Baptist Hospital and served his residency at City Hospital in St. Louis. He enlisted in the U.S. Army in December 1941 and rose to the rank of captain in just two years. Following his military service during World War II, he practiced medicine in Elsberry MO for more than 45 years, retiring in 1991. He is survived by his sister, son, two daughters, six grand-children and one great-grandson.

Mary K. Blaha, NU 39
Blaha died on April 18, 2006, in Marshalltown IA.

Seymour Brown, LA 40, MD 40
Brown, a St. Louis pioneer in anesthesiology, died on July 3, 2006, at St. John's Mercy Medical Center from respiratory failure.
He became interested in anesthesiology during his time in the U.S. Navy as a ship's physician, when at times he needed to practice medicine in trying conditions. He served as St. John's chief of anesthesiology for 40 years and was among the first in St. Louis to make regular pre- and post-anesthesia patient rounds. He also helped popularize advances in Caesarean section deliveries. Brown is survived by his wife of 65 years, Rose Tropp Brown, his son, Donald E. Brown, a granddaughter and two sisters.

Edward H. Kowert, LA 40, MD 43 (December)
Kowert died on June 10, 2006. He is survived by his wife, Marguerite Kowert, three daughters and a granddaughter.

Ernest T. Rouse Jr., MD 43 (March)
Rouse died of a heart attack on July 9, 2006, at his farm in Clarksville MO. He was 86. After serving in the U.S. Army Medical Corps during World War II as a physician and surgeon, Rouse was named chief of private service at Washington University School of Medicine. He later joined other doctors in forming the Clinic of Internal Medicine, one of the early incorporated physician groups in Missouri. In 1993, Rouse was honored with an Alumni/Faculty Award and named a professor emeritus of clinical medicine at Washington University School of Medicine. He is survived by his wife, Hope, four children, including Ernest T. Rouse III, MD 71, three stepchildren, 19 grandchildren and six great-grandchildren.

Harold H. Mitchell, MD 45
Mitchell died on June 25, 2006, at the age of 90 in Los Angeles CA.

Hugh R. Waters, MD 45
Waters died on July 12, 2006, of congestive heart failure at his home in Kirkwood MO. He practiced medicine for more than 45 years and was an instructor in clinical medicine at Washington University School of Medicine from 1953 until his retirement in 1990. He is survived by his wife, Margaret Donk Waters, a son, two stepdaughters and six grandchildren.

N. Balfour Sionim, MD 46
Sionim died on March 23, 2006, in Aurora CO. He is survived by his wife, Francisca, and siblings, Arthur and Leslie.

Winifred Heuser Hudak, NU 47
Hudak died on May 29, 2006. She was 85.

Ralph H. Forrester, MD 49
Forrester died on Feb. 1, 2006, at the age of 81. He was drafted into the U.S. Navy in 1942 and accepted in a pre-medical Naval Training Program in 1943. In 1945, he entered medical school at Washington University School of Medicine. After graduation, he transferred to the U.S. Army and continued his medical military career for another 20 years. Following retirement from the military, he joined the staff of the University of Texas Health Science Center as a professor of medicine and later became chief of staff at Audie Murphy Veterans Hospital. He is survived by his wife of 60 years, Dorothy, their five children, eight grandchildren, and nine half brothers and sisters.

Albert Goldstein, MD 50
Goldstein died on May 6, 2006, at Pomona Valley Hospital Medical Center, the same facility where he had helped bring thousands of babies into the world. His medical career spanned five decades and was marked by his good humor and incredible generosity toward the poor and needy, charging only a few dollars for each visit to his private practice in Pomona CA and volunteering his time whenever possible.

Betty S. Basinger, PT 53
Basinger died on Jan. 26, 2006, at the age of 75.

William H. Andrews Jr., HA 54
Andrews died on March 2, 2006, at the age of 86. He served as director of Cleveland Metropolitan General Hospital and then as senior vice president of the Cuyahoga County Hospital Systems. He was a life member of Kappa Alpha Psi, past president of the Cleveland-West Rotary Club, and a tennis enthusiast. He is survived by his wife, Mildred; son, William Henry III; and daughter, Brenda Joyce.

George Richard Keskey, MD, HS 57
Keskey died on Dec. 27, 2005, in Escanaba MI. He is survived by three sons, four daughters and one brother.

Ben Calvin Harmon, MD 60
Harmon died in his home on March 22, 2006, at the age of 71. He served as president of his class while a medical student at Washington University School of Medicine. Shortly after graduation, he was drafted into the Vietnam War, which was the beginning of his career as a military physician. He is survived by his wife, Jakie, three sons, one daughter, two grandsons, two granddaughters, two step-grandsons and two sisters.

Phyllis Schuessler, PT 62
Schuessler died on April 29, 2006. She is survived by her husband, Ted, two daughters, Julie Hogan and Linda Deal, and four grandchildren: Joshua, Brendan, Erika and Justin.

Alan R. Cohen, MD 71
Cohen died on Jan. 17, 2006, of an accidental fall in his New Mexico home. He received his undergraduate and master's degrees from Vanderbilt University and later his Bachelor of Divinity from Harvard Divinity School. Following his graduation from Washington University School of Medicine, he did his psychiatry residency at the Harvard-affiliated McLean Hospital in Belmont MA. In 2002, he retired to Santa Fe NM. He is survived by two sons, a grandson and two brothers.

Faculty

Irene E. Karl, MD, PhD
Karl, a pioneer in the cause and treatment of sepsis and a world-renowned authority on muscle metabolism, died on July 7, 2006, at age 90. Karl was a research professor of medicine in the Division of Metabolism and earned accolades from her colleagues at the university for her scientific achievements as well as her caring personality. Irene and her husband, Michael M. Karl, MD, HS 40, were the first couple at Washington University to have an endowed professorship named in their honor — the Irene E. and Michael M. Karl Professor of Endocrinology and Metabolism in Medicine. In 2002, Karl was the first female scientist to receive the Jewish Federation Business & Professional Woman of Valor award. Both Karls received the Albert Einstein Award from Technion University, the Barnes Hospital Distinguished Service Award, and the Second Century Award from the School of Medicine.
Asa C. Jones, MD 42, has found that a charitable gift annuity is a great way to receive lifetime payments, generate a charitable income tax deduction, reduce capital gain tax and support the School of Medicine. With him is Keith H. Bridwell, MD 77, the Dr. Asa C. and Mrs. Dorothy Jones Professor in Orthopaedic Surgery.

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Anesthesiologist and "SkyDoc" Ralph Glasser, MD 81, of Springfield IL, checks out the view before parachuting out of a plane for a closer look. Skydiving since his medical school days, Glasser also is an accomplished aerobatic pilot, performing with the Trojan Horsemen, a six-plane aerobatic team, at air shows across the country. For more on this story, please turn to page 27.
Hair cells and hearing The chick cochlea contains 10,000 sensory hair cells (shown in green) which detect sound in a very similar fashion to their counterparts in the human ear. But unlike human sensory cells, the chick cells can quickly regenerate if damaged. Understanding the biological basis of this repair process may lead to methods for inducing regeneration in the human ear. For more on this story, please turn to page 8.