The cocktail conundrum
Now and Then  Above: 2001 graduates Shannon McElearney, MD, Joanna Oda, MD, and Lineo Thahane, MD, from left. The School of Medicine conferred 122 degrees on May 18: 102 students received the MD degree, 14 received the MD/PhD degree, and six received the MD/MA degree. Below: Reunion 2001 brought together 1986 classmates Maggie McCracken, MD, Alison Whelan, MD, associate dean for medical student education, and Michelle Butzer Ruby, MD, from left.
OUTLOOK

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CLASS NOTES

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2001!
William G. Powderly, MD, holds a colorful assortment of pills, which in various combinations make up the "cocktail," the therapy which has proven to be a lifeline for many people infected with HIV (green model). He and his colleagues at the School of Medicine's AIDS Clinical Trials Unit (ACTU) help patients manage the disease, while holding out hope for better treatments. The potent drug mixture allows people to live longer and healthier lives, yet its long-term consequences are just beginning to be understood. Examining the cocktail's powerful effect on the body is becoming a focus of AIDS research. For more on this story, please turn to page 12.
Academy elects Gordon as member

JEFFREY I. GORDON, M.D., the Alumni Professor and head of molecular biology and pharmacology, was one of 72 new members elected to the National Academy of Sciences on May 1, 2001. Election to the academy is considered one of the highest honors that can be bestowed on an American scientist or engineer, and its members are chosen in recognition of their distinguished and continuing achievements in original research.

Gordon is known for his research on gastrointestinal development and how gut bacteria affect normal intestinal function and predilection to certain diseases. His research may help scientists understand such common human diseases as inflammatory bowel disease, irritable bowel syndrome and stomach ulcers.

In addition, Gordon's lab has studied an enzyme, N-myristoyltransferase, that affects the functions of many cellular proteins and is required for the survival of fungi that cause systemic infections in humans with compromised immune systems.

Gordon also is director of the Division of Biology and Biomedical Sciences, which oversees all PhD and MD/PhD students in the biological sciences, and has mentored more than 60 young researchers.

Boxerman assumes leadership of HAP

STUART B. BOXERMAN, D.S.C., has been named director of the Health Administration Program at the School of Medicine. He had been serving as interim director of the program since July 2000, following the retirement of James O. Hepner, Ph.D.

Boxerman earned three degrees from Washington University. Two were in engineering—a bachelor's degree in 1965 and a master's degree in 1965. In 1970, he was awarded his doctorate in applied mathematics and computer science.

The Health Administration Program, founded in 1946, provides its students with a firm foundation in management integrated with a solid understanding of the health care field and its current delivery systems.
Gelberman named AAOS president

RICHARD H. GELBERMAN, MD, the Fred C. Reynolds Professor and head of orthopaedic surgery, recently became president of the 25,500-member American Academy of Orthopaedic Surgery (AAOS) at its 68th annual meeting and scientific sessions in San Francisco CA.

A member of the academy since 1981, Gelberman has served on more than a dozen of its committees and task forces. Most recently, he had been one of the organization's vice presidents. As president, he plans to initiate a new program designed to improve musculoskeletal care for the public through better education for doctors.

Gelberman also is chief of hand and wrist surgery and director of the hand and upper extremity fellowship training program at the School of Medicine, and is orthopaedic-surgeon-in-chief at Barnes-Jewish and St. Louis Children's hospitals.

He has had support from the National Institutes of Health for his research on dense regular connective tissue since 1976. He also has research interests in radius fractures, carpal instability and nerve injuries.

Gelberman is the author of more than 200 scientific manuscripts and has received many awards for his research. He has served on the editorial boards of several medical publications, and currently serves as a reviewer for the Journal of Bone and Joint Surgery and the Journal of Orthopaedic Research.

The AAOS is a not-for-profit organization that provides education programs for orthopaedic surgeons, allied health professionals and the public.

Mild cognitive impairment appears to be Alzheimer's disease

MOST PEOPLE DIAGNOSED with mild cognitive impairment (MCI) eventually develop Alzheimer's disease, researchers with the School of Medicine's Memory and Aging Project (MAP) have found. The results suggest that MCI, characterized by minor memory loss, is an early stage of Alzheimer's rather than a separate disorder.

"We were surprised to find that an unexplained memory deficit that is currently called MCI almost always turns out to be early Alzheimer's," says John C. Morris, MD, Harvey A. and Dorisnae Hacker Friedman Professor of Neurology, director of MAP and co-director of the Alzheimer's Disease Research Center. He is first author of a paper on the subject that appeared in the March issue of Archives of Neurology.

Researchers examined 404 people who had either mild memory loss or no memory problems and who volunteered for annual memory assessments at MAP between July 1990 and June 1997. The 227 individuals with MCI were placed into one of three categories: fairly confident, suspicious and uncertain. The categories reflected the researchers' degree of confidence that the subtle signs of memory loss might indicate the onset of Alzheimer's disease.

The volunteers were reassessed annually for up to 9.5 years. After five years, Alzheimer symptoms had developed in 6.8 percent of the healthy volunteers, 19.9 percent of the individuals in the uncertain MCI group, 35.7 percent of those in the suspicious group and 60.5 percent of those in the fairly confident group. By 9.5 years, all of the volunteers with the most severe form of MCI had developed the clinical symptoms of Alzheimer's.

Forty-two participants died before the end of the study and donated their brains for postmortem analysis, the only way to diagnose Alzheimer's disease with complete accuracy. Autopsies of 25 volunteers who originally were diagnosed with MCI confirmed that 21 had Alzheimer's disease.

Morris points out that these results are based on a select group of individuals who volunteered for memory research. "Even with that caveat, the findings are impressive," he says. Earlier diagnosis will help scientists develop more effective therapies for early intervention.
Teitelbaum is FASEB president-elect

STEVEN L. TEITELBAUM, MD, has been selected as the next president-elect of the Federation of American Societies for Experimental Biology (FASEB), effective July 1, 2001. FASEB is the largest coalition of biomedical research associations in the United States, representing 21 societies with more than 60,000 members.

Teitelbaum, who is the Wilma and Roswell Messing Professor of Pathology, will serve as the group’s president in 2002-2003. Also a pathologist at Barnes-Jewish Hospital and St. Louis Shriners Hospital, Teitelbaum sets a primary goal in his new role to promote federal funding of biomedical and life sciences research.

The mission of FASEB is to enhance the ability of biomedical and life scientists to improve, through their research, the health, well-being and productivity of all people. The organization serves the interests of these scientists, particularly in areas related to public policy.

The group also facilitates coalition activities among member societies and disseminates information on biological research through scientific conferences and publications.

PHARMACOGENETICS

Drug resistance found to vary by ethnicity

A genetic mutation affecting resistance to chemotherapy occurs more frequently in some ethnic groups than in others, according to a new study.

Researchers found that African and African-American populations included more individuals with the drug-resistant gene than Caucasian or Asian populations. This might help explain why some people of African descent respond poorly to chemotherapy.

The research was presented March 25, 2000, at the annual meeting of the American Association for Cancer Research in New Orleans.

“We now know that the genetic influence on drug resistance is not the same throughout the whole population,” says Howard L. McLeod, PharmD, associate professor of medicine, of pharmacology and molecular biology and of genetics. “Because of this work, we can try to solve the problem.”

McLeod, who led the international team of researchers from his previous position at the University of Aberdeen in the United Kingdom, specializes in pharmacogenetics, an emerging research field.

Margaret-Mary Ameyaw, MD, PhD, of the University of Aberdeen, is the study’s first author and will join the Washington University faculty later this year.

The mutation studied by McLeod and his colleagues changes production of a protein called P-glycoprotein, or PGP, a molecular pump that rids cells of drugs. When working correctly, PGP pumps chemotherapeutic drugs out of tumors, allowing the tumor cells to survive. This response is known as drug resistance.

The genetic mutation means the PGP pump stops working, allowing drugs to enter and kill tumor cells.

Working with collaborators in five countries, McLeod and his colleagues did DNA tests on blood samples from 1,280 people from 10 ethnic populations. They found that some populations were significantly more likely than others to contain the mutation. The groups of African descent—Ghanaian, Kenyan, African American and Sudanese—had the mutation significantly less frequently than Caucasian and Asian populations tested.

Because lack of the mutation is associated with higher expression of PGP and thus higher drug resistance, these findings mean that physicians may soon have the necessary tools for individualizing therapy, especially for people of African heritage. Extreme interventions, such as gene therapy, would not be necessary because an existing medication that chemically inhibits the PGP protein could be given to people found to overexpress PGP.
Students, faculty receive Academic Women’s Network 2001 awards

THREE STUDENTS AND TWO PROFESSORS recently were recognized for their achievements by the university’s Academic Women’s Network (AWN).

Each year, the AWN recognizes graduating students in either the MD or PhD programs at the medical school based upon their demonstrated outstanding leadership in service to or advancement of women within the community. This year’s Student Leadership Awards went to Leah Bernstein, PhD, Emily Cronbach, MD, and Alison Stuebe, MD.

Bernstein published two first-author publications and contributed to a third during her graduate work in neuroscience. Her thesis project focused on the localization and regulation of the so-called RGS proteins or Regulators of G protein Signaling. Additionally, she has been active in neuroscience education and in student government.

Cronbach is a summa cum laude graduate of San Francisco State, with a bachelor’s degree in film. Prior to entering medical school, she worked on several documentaries related to teenagers and HIV. She was the co-organizer of the Reproductive Options Education program, a forum for debate on ethical issues in reproductive health, and she served as co-coordinator of the student chapter of the American Medical Women’s Association (AMWA), through which she developed a fourth-year elective in outpatient women’s health. She was selected for Alpha Omega Alpha, the national medical honor society.

Stuebe is a summa cum laude graduate of Duke University who came to Washington University after a stint as producer for the New York Times online site on women’s health. She was awarded the School of Medicine’s Mr. and Mrs. Spencer T. Olin Fellowship for Women, and also was selected for Alpha Omega Alpha. Stuebe was instrumental in creating the School of Medicine’s career counseling web site, which she presented at the 1999 American Association of Medical Colleges (AAMC) national meeting. She was active as co-coordinator of the student chapter of AMWA, and served on the group’s national web site task force.

The AWN presented its 2001 Mentor Awards to two faculty members: Linda B. Cotler, PhD, and Herbert W. Virgin IV, MD, PhD.

Cotler, professor of psychiatry (epidemiology) joined the Washington University faculty in 1990. She received her MPH from Boston University School of Public Health in 1980 and her PhD from Washington University in 1987.

Virgin is an associate professor in medicine, in molecular microbiology and in pathology and immunology. He received his MD/PhD from Harvard University and joined the Washington University faculty in 1991.

Outstanding Student Researcher

Third-year medical student Clint Walker (center) receives the Alpha Omega Alpha (AOA) 2001 Student Research Fellowship Award from Scot G. Hickman, MD, (left) professor of medicine and president of the School of Medicine’s AOA chapter. Walker was awarded $3,000 in support of his research on peripheral nerves. His advisers on the project are fellow John Winograd, MD, (right) and Susan E. Mackinnon, MD, professor and head of the division of plastic and reconstructive surgery.
Neufeld recipient of Rudin glaucoma prize for work in protecting nerve cells

ARTHUR H. NEUFELD, PHD, the Bernard Becker Research Professor of Ophthalmology and Visual Sciences at the School of Medicine, has been awarded the 2000 Lewis Rudin Prize by the New York Academy of Medicine. The Rudin Prize is given annually for outstanding glaucoma research published during the previous year.

Neufeld showed that protecting retinal nerve cells can help prevent damage in a chronic model of glaucoma.

In a 1999 paper in the Proceedings of the National Academy of Sciences, Neufeld and colleagues reported on experiments involving an animal model of glaucoma. Working in rats with elevated eye pressure, they were able to prevent loss of retinal ganglion cells by inhibiting the action of an enzyme that makes nitric oxide.

With co-authors Akira Sawada, MD, and Bernard Becker, MD, Neufeld demonstrated that an agent called aminoguanidine significantly limited retinal ganglion cell loss. Aminoguanidine inhibits the activity of the enzyme that makes nitric oxide, called inducible nitric oxide synthase (NOS-2).

Glaucoma, a disease in which patients first lose peripheral and then central vision, affects more than 3 million adults and is the second-leading leading cause of irreversible vision loss in the United States. More than 80,000 Americans with glaucoma are legally blind from the disease, and it is the No. 1 cause of blindness in African Americans.

Neufeld has received many grants from the National Institutes of Health to support his research. Currently, he is principal investigator on the grant, "Pharmacological Neuroprotection in Glaucoma," which has been helping to support his research aimed at inhibiting NOS-2 in the eye.

Over the last two decades, Neufeld has served the Eye Research Institute of Retina Foundation in a variety of capacities, including director of research. He also is a member of the Glaucoma Foundation's Scientific Advisory Board. He sits on the editorial board of the Journal of Ocular Pharmacology and Therapeutics, and he is a longtime member of the Association for Research in Vision and Ophthalmology, serving both as a trustee and as that group's president in 1984.

The Rudin Prize was established in 1995 and is funded by the Samuel and May Rudin Foundation.
New Center for Advanced Medicine names Walker, Tucker co-directors

Rose A. Walker and Kimberly Tucker will team up to direct the Center for Advanced Medicine (CAM), the new ambulatory care center scheduled to open in November 2001. Walker will represent the School of Medicine, and Tucker will represent Barnes-Jewish Hospital.

In her new position, Walker will coordinate clinical operations and policies with the 14 clinical centers housed in the Center for Advanced Medicine. She will work with Tucker on issues that cross institutional and departmental management lines, such as service issues affecting patients. As a liaison, she will assist patients or faculty members with concerns that arise among departments or between the medical school and the hospital.

Walker, who played a critical role in developing the Center for Advanced Medicine, also is director of ambulatory operations for the Faculty Practice Plan. She formerly worked as a nurse clinician and a nursing administrator for inpatient and ambulatory services at Barnes-Jewish Hospital and as a physician practice administrator for the medical school.

Tucker will coordinate the center's operational responsibilities related to Barnes-Jewish Hospital. She will establish standards of practice and care and develop policies and procedures in collaboration with Walker.

A clinical manager, Tucker has been in management at Barnes-Jewish Hospital since 1987. She earned a bachelor's degree in nursing from the University of Missouri-St. Louis, and she is completing a master's degree in nursing from the Jewish Hospital College of Nursing and Allied Health. Additionally, Tucker has served in leadership roles for the American Association of Critical Care Nurses and is a member of the American College of Health Care Executives.

First Guze Symposium held

The Missouri Alcoholism Research Center (MARC) recently hosted the first Guze Symposium to discuss the latest in clinical practices, research, and treatment for alcoholism.

The Guze Symposium was named in honor of the late Samuel B. Guze, MD, a pioneer of the medical model of psychiatric illness and in the field of alcoholism research. His early studies of alcohol use and abuse were important in the movement to consider alcoholism a disease rather than a character flaw.

Guze joined the faculty in 1951 and later served as vice chancellor for medical affairs and president of the Washington University Medical Center from 1971 to 1989. He also served as head of psychiatry from 1971 to 1989 and again from 1993 to 1997.

The symposium featured local and national experts on topics such as genetic studies of alcoholism, the role of depression and anxiety disorders in alcoholism, treatment for alcoholism and drug abuse, and the consequences of alcohol abuse by adolescents.

Created by a $6.7 million grant from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) at the National Institutes of Health, the MARC is one of 15 NIH-funded alcoholism research centers.

Housed at Washington University, the center also involves investigators from Saint Louis University, University of Missouri-Columbia, St. Louis and Palo Alto CA Veterans Administrations, and the Queensland Institute for Medical Research in Brisbane, Australia.
An age-related disease that compromises your most critical vision responds to a promising new therapy
by Candace O'Connor

For an older adult like Dorothy Beimfohr, who loves to read and needs to drive, age-related macular degeneration (AMD) is a terrifying diagnosis. “When I first heard that, it really just shook me,” she says.

How would this eye disease—in which abnormal blood vessels creep under the center of the retina, leaking blood and destroying vision—change her life? Would it curtail her pleasant visits to the Mascoutah, Illinois library? Would it rob her of the sight of her five grandchildren?

Patients with macular degeneration may lose the ability to clearly see these lines—and the things they love in life—even overnight.

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“When patients lose their center of vision, you can’t tell by looking at them that they are handicapped,” says Nancy M. Holekamp, MD, assistant professor of clinical ophthalmology, who treated Beimfohr.

“But they won’t recognize you because they can’t see your face, they have a hard time dialing your phone number and if you ask them to read something, they can’t. Consequently, they lose a lot of their independence.”

This disease, the leading cause of blindness in people 65 and older, is not only devastating for patients—it also is frustrating for their physicians. AMD sufferers, who otherwise may be in perfect health, become so desperate that they sometimes resort to sham treatments in an attempt to find a cure. And ophthalmologists, armed with few clinical weapons to fight the disease, have little they can do to help.

At the Barnes Retina Institute (BRI), a national leader in retinal research, Washington University faculty members are involved in several clinical trials that are testing new therapies aimed at saving or restoring vision in AMD patients. In fact, BRI faculty members have participated in most of the major trials that have taken place over the past several decades. A recent trial that examined a new approach to treating AMD, photodynamic therapy, has shown promising results.
When the center of sight fails

The center of the retina, called the macula, is highly detail-sensitive, allowing you to read this page or recognize your friend's face. Macular degeneration attacks this critical area of vision.

"Dry" AMD

AMD comes in two basic forms. The "dry" type is characterized by spots called drusen and sometimes by atrophy of the tissue layer that underlies the retina. No treatment exists for dry AMD, but it is also a milder, more slowly progressive disease that only accounts for 10 percent of severe vision loss among AMD patients.

"Wet" AMD

The story is much different with the second, "wet" form of the disease, in which blood and fluid from abnormal blood vessels leak onto sensitive photoreceptors in the macula. Among AMD patients, this type of the disease accounts for 90 percent of all severe vision loss. Often, this change occurs suddenly, without warning.

It is not yet known exactly why this happens. Attempts to link AMD to smoking or diet have not been successful. It is rare in Asian and African-American patients and most common in women 60 and older of Scandinavian descent. There may be a hereditary component to the disease—but what stands out is its correlation with age. The longer you live, the more likely you are to develop it.

Searching for effective treatment

"We see thousands of patients a year with macular degeneration; they make up at least 25 percent of our case-load," says M. Gilbert Grand, MD, professor of clinical ophthalmology. "This is a very significant problem, and we are continuing to see more of it as the population ages. Among the saddest aspects has been having to tell patients that we have limited forms of treatment."

In the late 1980s and early 1990s, Washington University and other institutions participated in the Macular Photocoagulation Study, sponsored by the National Institutes of Health, which targeted patients with wet AMD. The first phase of this trial focused on patients whose blood vessels had penetrated the macula but had not yet reached the fovea, its tiny, 500-micron-wide center.

In the study group, clinicians used a conventional, thermal laser to destroy the vessels; in the control group, patients did not receive laser treatment. The results showed that laser therapy was effective, but it was not a perfect solution. Nearly 50 percent of the time the vessels grew back—and the laser was destructive, creating a blind spot where it did its work.

Still, the results were positive enough that researchers went further, studying patients whose blood vessels had grown into the fovea. The laser treatment again yielded mixed results. It destroyed the blood vessels and stymied their regrowth, but it also destroyed the center of vision, rendering patients legally blind. Even so, 18 months after treatment, the treated patients were better off than the untreated control group.
Nancy M. Holekamp, MD, examines the eye of patient Sametta House.

About the same time, two Washington University ophthalmologists—Matthew A. Thomas, MD, of the BRI, and former department head Henry J. Kaplan, MD—pioneered an extraordinary form of surgery in which they elevated or focally detached the retina, plucked out the errant blood vessels, and then put the retina back in place. A multicenter clinical trial currently in progress, with Thomas as national vice chairman, is evaluating the success of this surgery, but it appears so far that it works best in younger patients.

Other trials are ongoing. A national, NIH-sponsored study—the Complications of AMD Prevention Trial (CAPT) —with Grand as principal investigator, is studying the use of low-power laser to treat dry AMD, which can be a precursor to the wet form of the disease.

BRI physicians also are participating in a study of macular translocation surgery, developed at Johns Hopkins. And they are enrolling patients in a trial sponsored by Alcon Research, Ltd., to see whether a new compound, anecortave acetate, stops the leakage from these abnormal blood vessels.

Photodynamic therapy may be one answer

But the latest and most promising form of AMD treatment is the photodynamic therapy (PDT) that Dorothy Beimfohr underwent, in which a non-thermal laser targets leaky blood vessels.

Washington University participated in the clinical trials of PDT, which was approved by the FDA in April 2000 for one form of AMD. Already, BRI physicians use it daily, and that usage may soon increase, since the FDA is on the verge of approving its use in other forms of AMD. In addition, PDT has strong potential for treating patients with other retinal diseases.

Beimfohr is delighted with the outcome of her PDT treatment. While many patients have bilateral disease, her left eye has not been affected. But the vision in her diseased right eye has improved from 20-80 to 20-40—enabling her to drive once again.

"PDT is an ingenious idea," says Holekamp. "The eye is set up perfectly for this type of novel therapy. And it only destroys the abnormal blood vessels without hurting the retina, which is a huge advantage."

The treatment is easy, quick and painless. The trick is to catch patients when they are just beginning to lose vision, since those who have had the disease for years— and have formed retinal scar tissue —will not benefit from any currently available treatment.

Retina specialists initially perform a fluorescein angiogram test to determine which patients are eligible for PDT treatment.

When Beimfohr came in for her PDT treatment, she received a 10-minute infusion of photoporphyrin dye, Visudyne™, into a vein in her arm. The dye coursed through all the blood vessels in her body, including the abnormal vessels in her retina. Then Holekamp shone the non-destructive laser at her eye for 83 seconds. Throughout the procedure, Beimfohr was fully awake; afterwards, she only had to avoid direct sunlight for five days.

Following treatment, ophthalmologists retest PDT-treated patients at three-month intervals to determine whether any regrowth has occurred. If it has, they repeat the treatment.

Beimfohr was fortunate—not only did the photodynamic therapy prevent the abnormal blood vessels from returning, her vision actually improved.

In the clinical trial of PDT, 67 percent of patients who received the treatment were stabilized or improved by it. Only 16 percent, however, had a return of good vision.

"So it is not the cure that we were hoping for," says Holekamp, "but it is something else that we have to offer patients who otherwise have no hope."
The cocktail

The standard treatment for AIDS is a potent multi-drug “cocktail” that successfully checks this deadly viral assault on the immune system.

Unfortunately, it’s getting harder to swallow.

BY GILA Z. RECKESS
WHEN FIRST DIAGNOSED WITH HIV IN 1990, Heidi Beddingfield was a carefree 18-year-old, still feeling the invincibility of youth. “I expected I only had three years to live, but it didn’t bother me,” she says. “After all, what could I do about it?”

She was right — there wasn’t much that could be done at the time. The few available drugs could only be expected to control the virus for about a year. Besides — it was too much of a hassle for the teenager to deal with grinding up multiple pills every day and sticking to a strict regimen.

In a way, she was lucky. Beddingfield’s virus didn’t flare up until December, 1995. Overnight, she went from feeling invincible to becoming incapacitated by a bacterial infection that attacked her brain, a not uncommon consequence of an immune system weakened by HIV. Fortunately, by that time, scientists had just discovered a new way to treat the disease: by combining three classes of medication.

After five weeks on this triple-drug cocktail, Beddingfield’s viral count decreased drastically; after a couple more weeks her virus qualified as “undetectable.” Six years later, her AIDS is still under control.

But there’s a catch. In 1998, Beddingfield started to dramatically lose weight. Her body is wasting away, and doctors now suspect the very drugs saving her life are to blame.
When the first cocktail component (nucleoside analogs, such as AZT) was introduced in 1987, scientists were optimistic. But patients with human immunodeficiency virus (HIV), the precursor to acquired immunodeficiency syndrome (AIDS), stopped responding to the medication after just one year of continuous use.

In the following years, two new classes of drugs were quickly approved by the FDA: non-nucleoside reverse transcriptase inhibitors and protease inhibitors. By 1995, the FDA recognized that combining drugs from these three classes crippled the virus' ability to replicate. The result: highly active antiretroviral therapy (HAART), commonly known as the AIDS drug cocktail.

Thanks to the cocktail, people with AIDS now are living considerably longer and healthier lives than before. But the treatment falls short of physicians' initial expectations. The new drugs may be able to control the virus, but they cannot eliminate it. Researchers have thus far conceded that patients will have to remain on medication for the rest of their lives. And, as has happened with the first cocktail component when taken alone, continuous long-term use of the cocktail could result in the development of drug-resistant strains of the disease, if patients don't adhere strictly to the drug regimen.

The drugs also may not be risk-free, as previously thought. As patients like Heidi Beddingfield live longer with the disease and spend years taking these drugs, new problems arise.

"Not until my body started to change did I really feel all the things AIDS robs you of," says Beddingfield, "your dignity, your self-esteem, your appearance and your physical well-being."

It's that last quality—physical well-being—that her School of Medicine physicians are focusing on. For 14 years, the university's AIDS Clinical Trials Unit (ACTU), part of the largest consortium of AIDS research centers in the world, has been at the forefront of developing new therapies. In 1997, experts here and at other centers started to notice a dangerous pattern of metabolic changes, such as insulin resistance and high cholesterol; today, these changes are found in roughly half of all patients on the cocktail. If these effects, collectively termed lipodystrophy, continue to intensify as expected, researchers predict persons taking the cocktail will eventually experience a marked increase in life-threatening complications such as diabetes, heart disease and stroke.

Patients with lipodystrophy exhibit at least two of the disorder's three main symptoms: insulin resistance, the precursor to diabetes; high triglycerides or cholesterol, which often leads to heart disease and stroke; and a unique pattern of fat distribution. Patients with the disease lose fat from their extremities and their faces, and they gain fat inside the abdomen itself, instead of just below the skin surface and outside the abdominal wall, as in normal weight gain.

The exact cause of lipodystrophy is unclear. What is known is that HIV makes copies of itself which then invade other cells. The virus recruits each corrupted cell along the way in a pattern of continuous replication. As patients live longer with the cocktail's help, the virus has more time to wreak havoc. Also, many HIV-positive patients are co-infected with other diseases such as Hepatitis B. As they survive longer, these secondary infections also have more time to affect metabolism.

But neither of these theories fully explains the sudden increased incidence of lipodystrophy noted in
the past few years, coincident with introduction of the third cocktail component, protease inhibitors.

“We believe that the body takes a series of hits,” explains Kevin E. Yarasheski, PhD, associate professor of medicine, “and that the toxic effects of the anti-HIV drugs and infection with HIV accumulate over the course of the disease.” Scientists propose that protease inhibitors in and of themselves do not cause lipodystrophy. But, when taken in conjunction with this sequence of “hits,” they may trigger undesirable physical and biochemical changes in the body.

Researchers at the ACTU decided to take action. William G. Powderly, MD, co-director of the division of infectious diseases and professor of medicine, assembled a team led by himself, Yarasheski and Samuel Klein, MD, the Danforth Professor of Medicine and Nutritional Science, to investigate this emerging problem. The team plans to analyze muscle and fat tissue samples from lipodystrophy patients and compare them with samples obtained from HIV-infected individuals who are not experiencing metabolic changes. They also will examine the contribution of protease inhibitors to these metabolic changes by carefully altering the components of the cocktail in certain individuals experiencing side effects.

Further insight into the lipodystrophy phenomenon may provide new hope for patients infected with HIV and for non-infected individuals with diabetes, high cholesterol or triglycerides, or abdominal fat.

“If we determine the mechanisms underlying the cause of lipodystrophy in HIV-infected patients, we may be able to develop specific therapies for these complications or, even better, help to design drugs that target the virus but avoid these effects,” says Powderly. “The other spin-off is that this is a model system for very common disorders, such as diabetes and high cholesterol, in individuals who are not HIV-positive. We can use these new drugs to gain a glimpse of metabolic processes in normal, healthy individuals that we otherwise might not have found.”

Washington University researchers already have made the novel discovery that patients who receive the drug cocktail are more susceptible to bone softening, such as that which occurs in osteoporosis. Steven L. Teitelbaum, MD, the Wilma and Roswell Messing Professor of Pathology, specializes in the basic science aspect of bone research. Already he is using information from the ACTU’s clinical research to study the effects of HIV on bone cells in mice.

The School’s clinical AIDS care could soon stretch from St. Louis to Ethiopia

Washington University School of Medicine not only has one of the leading AIDS research programs, it also serves the St. Louis community through various outreach efforts. One example is the Helena Hatch Special Care Center for women with HIV, which has become a nationally recognized center of excellence for comprehensive HIV care and clinical investigations of HIV among women.

Soon, the School of Medicine’s influence may reach as far as Africa, where availability of the latest medications and information is still scarce despite the fact that more than 25 million people there are now infected with HIV.

David B. Clifford, MD, and his African research fellow, Enawgaw Mehari, MD, recently returned from a trip to Mehari’s home country, Ethiopia, where they discussed plans for a clinic at the University of Addis Ababa. With funds from organizations such as the World Bank, the United Nations and the National Institutes of Health, the team hopes to establish a center at the university where they will mentor Ethiopian physicians and establish a basic AIDS therapy program.

“We’re excited about the possibility of setting up a clinic which will be a practical help to people who are in desperate need,” says Clifford. “Ever the academician, I also am eager to have the opportunity to learn more about this infection in a different cultural population. We’re hopeful that it will be a very rewarding project.”

Ethiopian artist Afewerk Tekle created “Unity Triptych,” internationally famous stained-glass windows that confront visitors in the entrance of Africa Hall, headquarters of the United Nations Economic Commission for Africa, in Addis Ababa, Ethiopia. The piece embodies in three panels Africa’s sorrowful past, present struggles and high aspirations for the future.
During the first five years of living with her disease, Heidi Beddingfield neglected to take her medications. Even with today's improvements in AIDS therapeutics, she ingests a grueling regimen of 30 pills a day. Imagine how much more difficult it would be to keep up with this rigid schedule for patients who also are developing neurological symptoms such as memory loss or attention difficulties.

Despite treatment advancements, some patients are faced with this added challenge. Within days of being infected with HIV, the virus spreads into the central nervous system (brain and spinal cord) and into peripheral nerves. In fact, it is puzzling that only some patients experience the effects of nervous system damage. By understanding these symptoms and determining how and when they arise, researchers hope to improve their basic understanding of AIDS and to develop new ways to treat the infected nervous systems.

Just as in lipodystrophy, some neurological effects of HIV may be exacerbated by the toxicity of medications. For example, peripheral neuropathy—chronic, disabling pain in peripheral nerves such as those in the feet—actually worsens with treatment of the virus and is estimated to affect at least 30 percent of patients with AIDS. In contrast, the incidence of central nervous system disorders has decreased since the cocktail was introduced, from roughly 65 percent to less than 10 percent.

"The numbers are down, but it's still a serious problem," says David B. Clifford, MD, the Seay Professor of Clinical Neuropharmacology in Neurology and vice chairman of neurology. "Our main concern is what will happen next, because we know this is an area where the virus is just waiting to spring back and where our therapies are incomplete."

The central nervous system arguably presents the biggest challenge in understanding how to reach the virus and halt its destructive effects. Medications have a difficult time getting into the brain because of its natural protective shield, the blood-brain barrier. Also, scientists suspect that HIV attacks the brain and spinal cord in a slightly different fashion than the rest of the body.

Clifford therefore is examining the cerebrospinal fluid—fluid that fills the spaces around the spinal cord and in the brain—from HIV-positive patients. He plans to measure the activity of the virus in the central nervous system as cognitive performance changes and hopes to determine the effectiveness of HIV medications in penetrating and helping the nervous system.

Another unique challenge is that brain cells are more sensitive to changes in their environment than other cells in the body. According to Clifford, cognitive decline may result from the sheer presence of infected immune cells that release chemicals not normally found in the brain environment. His team currently is testing a promising drug called selegiline that may help protect nerve cells.

"Because we can't yet eradicate the disease, there is a low-grade infection in the brains of all patients with HIV," says Clifford. "We are concerned that as patients live longer, they may be subject to an accelerated degenerative disease, similar to Alzheimer's."

Despite these hurdles, one fact remains: These drugs save lives. According to Pablo Tebas, MD, medical director of the ACTU and assistant professor of medicine, "HIV is not a death sentence anymore. There is a trade-off in everything in life, and medicine is no exception. But the benefits of understanding the side effects of therapy will be global."
Colds and cancer are different, right?
But shouldn’t the body’s defensive gatekeeper—the immune system—guard against both?

Research stood in the face of common sense—until now.

BY GILA Z. RECKESS
Chicken soup may soothe the throat or calm an aching tummy, but the immune system ultimately is the body’s real hero, scouring it for danger and defending it against suspect cells. But what about tumor cells? Does the immune system also protect against these often deadly enemies?

For years scientists expected it did. But studies in the 1970s found that “nude” mice—those thought to lack immune cells called lymphocytes—did not develop more chemically induced or spontaneous tumors than normal mice. The immune system theory was largely abandoned.

But some researchers continued to search for a role of the immune system in tumor development, determined to bridge the gap between immunology and oncology.

To that end, Robert D. Schreiber, PhD, the Alumni Professor of Pathology and Immunology and professor of molecular microbiology, formed a collaboration with Lloyd J. Old, MD, director and CEO of the Ludwig Institute for Cancer Research at Memorial Sloan-Kettering Cancer Center in New York. Schreiber is known for his research on interferon-gamma (IFNγ), an important protein in the immune system, while Old is considered by many to be the grandfather of tumor immunology. With help from a team of School of Medicine researchers, the pair have determined that the immune system does in fact appear to protect against tumor formation.

Combined with mounting evidence in the field, it’s a discovery that could redirect the pursuit of cancer therapies and our understanding of how the human body responds to infection.

Four key findings: The immune system eliminates cancer therapies and our understanding of how the human body responds to infection.

Schreiber’s team first examined whether mice lacking lymphocytes developed tumors when exposed to a chemical carcinogen. To do so, they developed a strain of mice that definitively lacked functional lymphocytes. This was accomplished by inactivating a gene found in all lymphocytes, RAG2.

They then injected the chemical carcinogen MCA into a group of mice lacking RAG2 and into a group of normal mice. Only 19 percent of normal mice developed tumors, in contrast with 58 percent of RAG2-deficient mice.

In previous studies, the group examined the effect of MCA on mice lacking either the receptor for IFNγ or one of the proteins required for the receptor to function, Stat1. Roughly half of these mice also developed tumors.

In their current study, the researchers also generated mice with two disrupted genes—the gene for RAG2 and the gene for Stat1. When these doubly-deficient mice were injected with MCA, 72 percent of them developed tumors. Statistically, this was not greater than the incidence of tumors in mice that lacked just one gene or the other. Therefore, the team concluded that RAG2 and the IFNγ receptor have overlapping roles.

“We think the two are potentially part of the same mechanism but represent different steps in the process,” explains Schreiber. “IFNγ makes tumor cells expose themselves to the immune system. After seeing the abnormal proteins in the tumor, the lymphocytes eliminate the tumor cells.”

Lymphocytes and IFNγ help prevent formation of chemically induced tumors

Even a healthy immune system only catches some tumors—those that escape detection pose a greater threat

As a result of protecting the body, the immune system paradoxically favors the outgrowth of tumors that are less likely to be recognized and killed by the immune system,” Schreiber says. “It’s a ‘survival of the fittest’ scenario that works against the host.”

His immunoeediting theory may explain this selective protection. “If immunoediting is always occurring, it can have multiple outcomes,” he explains. “If you’re lucky, the outcome is protection. But if you’re unlucky, transformed tumor cells might alter themselves so the immune system can pick out only a few. The others continue growing.”
only some human tumors can be directly blamed on chemical carcinogens. Often, tumors develop spontaneously, without any apparent trigger. So Schreiber and colleagues examined whether lymphocytes and Stat1 contribute to the natural development of tumors in the absence of a carcinogen.

Again, they studied three groups of mice—normal, RAG2-deficient, and those deficient in both RAG2 and Stat1.

After 15 months, two of 11 normal mice had noncancerous tumors and the rest were tumor-free. On the other hand, all 12 RAG2-deficient mice had developed tumors, half of which were cancerous.

Lymphocytes and IFNγ help prevent formation of spontaneous tumors

Some tumors that escape immune detection appear to have low levels of a protein called TAP1. So the scientists added this protein to tumors before transplanting them into healthy mice. This, they hoped, would trick the immune system and allow for easier identification of dangerous cells.

When highly aggressive tumors such as those that managed to develop in mice with a healthy immune system were transplanted into RAG2-deficient mice, they still went unnoticed. Thus, TAP1 facilitated tumor detection and elimination only in the presence of a healthy immune system.

"We showed that if a tumor is forced to reveal itself to the immune system, it often is rejected," Schreiber explains. "We think that a tagged tumor could be used to train the immune system to reject others like it. This is very exciting because it indicates that immunotherapy has a significant potential use even for the treatment of tumors that are altered by the immunoediting process."

TAP1 can flag tumors, making them more "visible" to the immune system

When tagged tumors were transplanted into RAG2-deficient mice, they still went unnoticed. Thus, TAP1 facilitated tumor detection and elimination only in the presence of a healthy immune system.

"We showed that if a tumor is forced to reveal itself to the immune system, it often is rejected," Schreiber explains. "We think that a tagged tumor could be used to train the immune system to reject others like it. This is very exciting because it indicates that immunotherapy has a significant potential use even for the treatment of tumors that are altered by the immunoediting process."

The first flaw in the evidence against the immune system theory was revealed in the mid-1980s, when two separate studies found that nude mice were not in fact completely free of lymphocytes, as previously thought.

Schreiber and others later found signs that both lymphocytes and IFNγ might play important roles in tumor prevention.

Now, in a paper published in the April 26, 2001 issue of the journal Nature, Schreiber’s team presents the first conclusive evidence that lymphocytes and IFNγ work together to find and eliminate tumor cells.

When a role for the immune system in tumor formation was proposed decades ago, scientists envisioned a process called immunosurveillance. Like a burglar alarm that detects intruders, the immune system was thought to patrol the body, catching cells at the beginning of their transformation into suspicious tumor cells.

In contrast, Schreiber and his colleagues propose a new model called immunoediting. Like the security guard, editors catch errors and delete them. They also adjust and tweak areas that need smaller alterations. According to immunoediting, the immune system constantly eliminates certain types of tumor cells and also changes the characteristics of others.

"This sheds light on an age-old controversy and suggests new possibilities for cancer therapy," says Schreiber.

Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Lymphocytes</td>
<td>White blood cells (immune cells) that detect and kill foreign or diseased cells</td>
</tr>
<tr>
<td>RAG2</td>
<td>Gene found in all lymphocytes</td>
</tr>
<tr>
<td>IFNγ</td>
<td>Protein produced by lymphocytes that helps the immune system</td>
</tr>
<tr>
<td>Stat1</td>
<td>Protein required for IFNγ to function</td>
</tr>
<tr>
<td>TAP1</td>
<td>Protein found in low levels in many tumors that escape immune system detection</td>
</tr>
<tr>
<td>Doubly-deficient</td>
<td>Mice lacking RAG2 and Stat1</td>
</tr>
</tbody>
</table>
SMILE

DOCTOR

For many children, and indeed many adults, a dentist’s office is a place of dread. But in the pastel-colored waiting room of Donald V. Huebener, DDS, MS, at St. Louis Children’s Hospital, the mood is upbeat. Kids try out the miniature chairs and flip through pop-up books. They laugh and chatter with their parents as if they were in line for a ride at Six Flags rather than waiting to see the dentist. One teenager takes a nap in his seat.

When it is 9-year-old Sean’s turn, he goes in to greet Huebener with a smile and a handshake. His mother, Dee Ann Godlewski, follows watchfully. “He’s always happy to see Dr. Don,” she says, “but when the chair leans back, he gets nervous. It’s only natural, after all he’s been through.”

Sean was born with a cleft lip and palate, and has had 18 surgeries in his young life. But Huebener, professor of plastic and reconstructive surgery who supervises the four dental residents and two assistants in pediatric dentistry at Children’s, has had plenty of experience putting children at ease during his 30 years at Washington University. He takes Sean through his checkup step by step, explaining what he is about to do and rewarding cooperation with compliments. Soon the visit is over, and Sean bounds from the chair with a big smile. “I’m done!” he booms. “Thanks!” There remains only a visit to the prize drawer, from which he selects a “stretchy alien guy.”

Not all of Sean’s visits go this smoothly, but his strong relationship with Huebener has guided him over the rough spots. “Dr. Don is wonderful with kids,” says Godlewski. “When he explains firmly what has to be done, Sean will giddy up. But he also has a soft touch when it’s needed.”

A cleft palate can impair a child’s hearing, speaking and eating. Huebener takes time with parents, explaining what he and other physicians and dentists must do to correct problems. “At each stage he’s told me: ‘After this procedure Sean will get better,’ and he always does,” Godlewski says.
Children with serious medical conditions require complex treatment, of which dental care is an important component. Unfortunately, it is often the missing component, because there are not enough dentists who are willing and able to tackle the challenges of caring for a special needs child. According to the American Medical Association, dental care is the greatest unmet need of these children.

Lisa Burbes could not find a dentist willing to treat her infant daughter, Hope, until Huebener stepped in. Hope had a congenital heart defect which would require four surgeries by the time she was 2 years old. She also was prone to cavities. Left untreated, they could provide a reservoir for contagion that threatened to spread.

"Dental caries (tooth decay) is an infectious disease," Huebener, professor of pediatrics, explains. "Bacteria may go through the enamel into the dentin, then into the nerve, and enter the bloodstream." If a child has a heart defect, the bacteria may lodge there and create problems. Hope now is 9 and has not needed surgery in five years. But she still requires vigilant dental care, because the re-routing of blood flow resulting from surgical correction also may make the heart vulnerable to bacteria. Hope doesn't mind the frequent visits. "She really likes the dentist" Huebener explains. "You have to be careful even about giving local anesthetics, because he may start to bleed from the needle stick." In such cases, Huebener has to consult with the child's pediatric hematologist about building up the appropriate coagulation factor in the blood before he goes to work.

Children with psychomotor disturbances, who are unable to stay still in the chair, may require sedation or general anesthesia, and so may very young children with extensive caries. Cerebral palsy patients also find it difficult to keep still, but Huebener has found that gently he often can work on them without general anesthetic.

The complex medical cases he treats provide Huebener and his colleagues with the opportunity to meet unique professional challenges. But it is his deft personal touch that allows him to be both doctor and friend to his young patients.
Dr. Don,” Burbes explains as Hope selects her prize (a ring, as usual). “His whole staff is good with children.”

Infection spreading from dental caries also is a threat to children with other medical problems. Before a child can receive an organ transplant, surgeons require a clean bill of oral health from Huebener. The drugs that prevent the immune system from rejecting the transplant also lower the body’s defenses against bacterial infection. Huebener’s current patients include three receiving hearts and one receiving a double-lung transplant, along with a number of children receiving liver and kidney transplants.

Cancer patients need meticulous dental care before and during chemotherapy, a treatment that causes their white blood cell count to go down, thus making them vulnerable to infection. Huebener works closely with their pediatric oncologists. “Any dental care—an extraction, a filling, even a routine cleaning, has to be timed with chemotherapy,” he explains.

Huebener sympathizes with parents who come to him after a long day of trudging from one specialist’s office to another.

“They’re overwhelmed with their child’s problems, and now they’re being sent to still another doctor,” he says. He remembers one mother of a very sick boy who came in feeling exhausted, discouraged and hostile. He sat down with her. “I told her, ‘I’m here to help you in any way I can. Your son’s problems are my concern.’ And as we talked, all the negativity went away. Now we’re the best of friends.”

Huebener believes in being completely honest with parents. He spends a lot of time with them, explaining their child’s condition and discussing treatment options. Lisa Burbes, Hope’s mother, notes that Huebener has spoken several times to her support group for families of children with heart defects.

Relationships with families of cleft-palate patients like Sean Godlewski become especially close because the course of treatment is long. “I had a 16-year-old in today whom I first saw as a baby,” Huebener says. “Over the years, you become a friend of the family.” Parents call frequently, seeking advice not just on medical care but on such issues as whether their child with a cleft deformity can go out for football or take up a wind instrument.

**GETTING PAST THE FEAR**

Asking the secret of his rapport with his young patients, Huebener smiles and replies: “Pediatric dentists are also psychologists. Patience is their middle name and good buddy is their game.” Contrary to popular belief, he observes, fear of the dentist is not a normal part of childhood. It arises because, all too often, parents wait until children have a mouthful of cavities to take them for their initial visit. Ideally, dental visits should begin when the first baby tooth comes in. “You build a relationship of confidence and trust, so that when you do have to give them local anesthesia for a filling, it’s not the end of the world,” Huebener says.

To put the young patient at ease, he talks as he works, explaining what he is going to do and why it is necessary. In this, he emulates his own fondly remembered childhood dentist, who let him play with the “gizmos and gadgets” in the office, and who made a dental checkup an occasion to look forward to. His interest sparked, Huebener went on to attend Washington University School of Dental Medicine. The school, which closed in 1991, had a fine department of pediatric dentistry, says Huebener, and it was the chair, Patricia Parsons, DDS, who inspired him to make children his life’s work.

“There’s always something to look forward to,” says Huebener, “something I haven’t seen before or helped a patient with. That’s what makes my job so fascinating.”
IT'S A MATCH! The annual match day was held on March 22, 2001, and 110 of the 123 graduating medical students took part in the National Resident Matching Program (NRMP).

One hundred percent of the match day participants secured a postgraduate training position. Some 57 percent received first-year residency positions at their first choice of institution and 80 percent matched to one of their top three choices. Eleven students found positions independent of the NRMP.

YEESAfffffff!!! Hyung Kim unbridles his enthusiasm.

ARIZONA

Phoenix
Barrow Neurological Institute
ORTHOPAEDIC SURGERY
Pankaj Gore

CALIFORNIA

Loma Linda
Loma Linda University
ER MEDICINE
Tania Shaw
SURGERY, PRELIMINARY
Matt Abrahams

Los Angeles
Kaiser Permanente, LA Program
INTERNAL MEDICINE
Peggy Shen
UCLA Medical Center
INTERNAL MEDICINE
Lauren Butwell
OB/GYN
Emily Cronbach
UCLA Neuropsychiatric Hospital
PSYCHIATRY
Joe Simpson
University of Southern California
DIAGNOSTIC RADIOLOGY
Hyung Kim

OPHTHALMOLOGY
Joanna Oda

Sacramento
University of California, Davis
FAMILY PRACTICE/OB, COMBINED
Melissa Marshall
INTERNAL MEDICINE
Vino Subramanian

San Francisco
University of California-San Francisco
INTERNAL MEDICINE
Deepu Nair
NEUROLOGY
Andy Josephson

San Jose
Santa Clara Valley Medical Center
INTERNAL MEDICINE
Dora Ho
INTERNAL MEDICINE, PRIMARY
Gina Serraoacco

Stanford
Stanford University Program
GENERAL SURGERY
Monica Tatania

TORRANCE
Harbor-UCLA Medical Center
ORTHOPAEDIC SURGERY
Chris Combs

TRAVIS AIR FORCE BASE
David Grant Medical Center
TRANSTITIONAL
Glen Macpherson

COLORADO

Denver
University of Colorado
INTERNAL MEDICINE
Kari Braun

DISTRICT OF COLUMBIA

Washington
National Capital Consortium
Walter Reed Medical Center
INTERNAL MEDICINE
Amanda Weeks

GEORGIA

Augusta
Medical College of Georgia
DERMATOLOGY
Dan Sheehan

ILLINOIS

Chicago
Children's Memorial Hospital
PEDIATRICS
Amy Bobrowski
(Elridge)
Zev Waldman
Rush Presbyterian/St. Luke's/Cook County Hospital
INTERNAL MEDICINE, PRIMARY
Emily Engelland
University of Chicago Hospital
INTERNAL MEDICINE
Shanika Samarasinghe
PEDIATRICS
Julie Bubek-Wardenburg

IOWA

Iowa City
University of Iowa Hospitals & Clinics
ORTHOPAEDIC SURGERY
Anthony Friella
Mike Huang

LOUISIANA

New Orleans
Ahon Ochsner Medical Foundation Program
INTERNAL MEDICINE/FAMILY PRACTICE, COMBINED
Kevin Sterling

MARYLAND

Bethesda
National Naval Medical Center
PEDIATRICS
Abigail Harmon
National Capital Consortium, Uniformed Services Program
OB/GYN
Belinda Blood
Boston
Beth Israel Deaconess Medical Center
  INTERNAL MEDICINE
  Alice Hsu
  Brigham & Women's Hospital
  INTERNAL MEDICINE
  Lynn Henry
  OB/GYN
  Alison Stuebe
  Harvard/Beth Israel Deaconess NEUROLOGY
  Jennifer Langdorf
  Harvard/MGH and Brigham & Women's NEUROLOGY
  Bob Balch
  Massachusetts General Hospital
  DIAGNOSTIC RADIOLOGY
  Dan Cohnen
  Bena Karp
  INTERNAL MEDICINE
  Ethan Kornegold
  PEDIATRICS
  Michael Kappelman
  New England Medical Center
  PEDIATRICS
  Jessica Sachs

Burlington
Lahey Clinic
  GENERAL SURGERY
  Jonathan Chan

Ann Arbor
University of Michigan
  ENT
  Marc Thorne
  OPHTHALMOLOGY
  Seth Silber

Detroit
Henry Ford Health Sciences Center
  ER MEDICINE
  Amy Stark

St. Louis
Barnes-Jewish Hospital
  ANESTHESIOLOGY
  Ken Cummings
  DERMATOLOGY
  Lawrence Wang
  DIAGNOSTIC RADIOLOGY
  Winch Chong
  ER MEDICINE
  Ann Young
  INTERNAL MEDICINE
  Ting-Hsu Chen
  Linda Cheng
  Jonas Cooper
  Mary Doi
  Tom Fong
  Dustin James
  Rachel Presti
  Shelby Sullivan
  Holly Magiera
  Geoff Uy
  INTERNAL MEDICINE, PRELIMINARY
  Michael Lam

Boston
St. Louis
Flushing
Catholic MC of Brooklyn & Queens
  OPHTHALMOLOGY
  Mohammed El-Bash

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  Rob Brophy
  Lenox Hill Hospital
  GENERAL SURGERY
  Cindy Yeoh
  New York Presbyterian Hospital
  Columbia
  OB/GYN
  Tessa Madden
  New York Presbyterian Hospital
  Columbia
  INTERNAL MEDICINE
  Ann Tilley
  INTERNAL MEDICINE, PRIMARY
  Sonal Shah
  New York University School of Medicine
  PSYCHIATRY
  Laura Rymarquis

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University Hospital of Cincinnati
  PEDIATRICS
  Tim Beukelman
  Cleveland
  Orthopaedic Surgery Foundation
  OPHTHALMOLOGY
  Albert Dakanho
  University Hospitals of Cleveland
  PEDIATRICS
  Joan Lee
  Amy McBee (Davis)

Columbus
Ohio State University Medical Center
  OB/GYN
  Shefali Gandhi
  Riverside Methodist Hospitals
  FAMILY PRACTICE
  Marianne Tietter (Willey)

Philadelphia
Children's Hospital of Philadelphia
  PEDIATRICS
  Linco Thahame
  Hospital of the University of Pennsylvania
  DERMATOLOGY
  Aimee Payne
  INTERNAL MEDICINE
  Carol Kaplan
  Schein Eye Institute / University of Pennsylvania
  OPHTHALMOLOGY
  Wai Wong
  Thomas Jefferson Hospital
  DIAGNOSTIC RADIOLOGY
  Lauren Woodruff
  University of Pennsylvania
  CHILD PSYCHIATRY (2002)
  Sharon Habashi
  NEUROLOGY
  Josh Habashi

Chapel Hill
University of North Carolina
  DERMATOLOGY
  Erin Long

Durham
Duke University
  INTERNAL MEDICINE
  Marc Drake
  NEUROSURGERY
  Lee Selenick

Akron
Akron General Medical Center
  ER MEDICINE
  Jason Kolb
  Summa Health System
  ER MEDICINE
  Samuel Lofgren

New York
Rochester
University of Rochester/ Strong Memorial
  DIAGNOSTIC RADIOLOGY
  Paul Kim
  ORTHOPAEDIC SURGERY
  Shawyon Shadman
  PEDIATRICS
  Katy Harrod-Kim

North Carolina
Chapel Hill
University of North Carolina
  DERMATOLOGY
  Erin Long

Durham
Duke University
  INTERNAL MEDICINE
  Marc Drake

OHIO
Akron
Akron General Medical Center
  ER MEDICINE
  Jason Kolb
  Summa Health System
  ER MEDICINE
  Samuel Lofgren

CheerS!!! Carol Kaplan
is pleased—greatly.
Richard A. Blath

It’s the ‘little things’ in life
Making a difference in the lives of individuals

The “LITTLE THINGS” are the big reasons why Richard A. Blath, MD ’71, finds his work very satisfying. Those little things may be grateful words from a patient whose cancer he has removed, or a phone call from a couple with fertility problems telling him the good news that the wife is pregnant, or the appreciation of parents whose child’s birth defect he has corrected. They are indications of the difference he makes in the lives of individuals. His other achievements and the leadership roles he fulfills are notable, but he views them as incidental to caring for his patients.

Blath, a urologist and surgeon, is Chief of Staff at Christian Hospital NE-NW in St. Louis and managing partner of St. Louis Urological Surgeons, Inc., a nine-member group with five offices in the metropolitan area. The group, a pioneer in the early use of brachytherapy in the Midwest for men with prostate cancer, has treated more than 300 such patients.

Before the approximately 500-member medical staff at Christian Hospital elected him chief three years ago, Blath, a Fellow of the American College of Surgeons, chaired the department of surgery there for 10 years. During that time, he initiated with Washington University School of Medicine a rotation for surgery residents that provides a wealth of training in general, vascular and trauma surgery. Residents have often rated it among the best of their experiences.

The success of the residency program prompted School of Medicine faculty to ask Blath to arrange a surgery clerkship for third-year medical students, the first such rotation at a hospital away from the Medical Center. Two students per month participate, and the clerkship is so popular that many more apply than can be accepted.

Blath takes pride and pleasure in helping residents and students broaden their education. He remembers appreciatively his own teachers during student and resident days at Washington University. Two who particularly inspired him were now Professors Emeritus Charles Manley, MD, HS ’63–’67, the first pediatric urologist in St. Louis, and Robert Royce, MD ’42. Blath calls Royce the “ultimate professional whose clinical skill and bedside manner you strive to emulate.”

A loyal alumnus ever since, Blath served as president of the Washington University Medical Center Alumni Association during 1995–96 and as a member of the Executive Council for a number of years. He has chaired class reunions and is a member of the Eliot Society.

As a child, Blath suffered from asthma and many respiratory and ear infections, which required frequent visits to his pediatrician, whom he respected greatly. That experience influenced him to choose medicine as his own career. He attended Miami University in Ohio, which had a cooperative agreement with Washington University permitting students to enter medical school after three years of undergraduate work. He was inducted into
As health care delivery has become more complex and more third parties are involved, Blath devotes more time to participation on policy-making bodies where he can be an advocate for patients and physicians. He chairs the Medical Executive Committee at Christian Hospital and is one of five representatives from Christian who sit on the Board of Directors of BJC. (He is the only independent private practice physician on that board.) Christian Hospital President Paul Macek comments that the hospital is “fortunate to have someone of Dr. Blath’s caliber in key leadership positions” and describes him as “a trusted advisor in dealing with the challenges we face.” Blath also serves on physician advisory panels of several major health insurers, including Blue Cross and United Health Care.

With all this, the best part of Blath’s day is “coming home to Lorry,” his wife, whom he describes as “the creative one.” A gourmet cook, an artist and a writer, she is currently working on a “semi-autobiographical” novel. The rabbi who married them in 1969 declared it a “marriage made in heaven” because they met in Lambert Airport when both were students returning to Miami University after the winter holidays. She had visited her parents in Amarillo TX, and had to change planes in St. Louis. Richard saw her struggling to carry her new stereo, went to assist, and they sat together during the flight. The rest is family history, which includes a married daughter living in Columbus who is the mother of their two grandsons, and a son, an artist living in Rhode Island.

A lover of adventure, Blath once spent his vacation on a cattle drive in Wyoming (as a boy, he wanted to be a cowboy). He has gone whitewater rafting on the Salmon River and in Costa Rica, skiing in Aspen and elsewhere. Last year he and Lorry went on safari in Africa, spending time in Zimbabwe and Botswana, a trip that allowed him to practice his considerable photographic skills. He also plays golf “poorly,” and, perhaps to assure that he will take time out of his busy life to smell the proverbial roses, he grows more than 25 varieties in the backyard.

Above: Richard A. Blath, MD, instructs third-year medical student Caitlin Aveyard.

Left: While on African safari, Richard and Lorry Blath visit breathtaking Victoria Falls in Zimbabwe.

Outlook Summer 2001

Alumni & Development 27
ALUMNUS DAVID CLAYSON, PHD, has bequeathed a professorship in neurology at Washington University in St. Louis. The chair will bear his name.

The announcement was made by Mark S. Wrighton, PhD, chancellor of Washington University, and William A. Peck, MD, executive vice chancellor for medical affairs and dean of the School of Medicine.

Clayson received his doctorate in psychology from the College of Arts and Sciences in 1963. He established the professorship to support scientists whose research is relevant to developing effective treatments of ALS and other neurodegenerative diseases.

"I am saddened by Dr. Clayson's terrible illness and death, but grateful for his humanity and generosity in making this wonderful gift," says Dennis W. Choi, MD, PhD, Andrew B. and Gretchen P. Jones Professor of Neurology and head of neurology at the School of Medicine.

Clayson was emeritus professor at the Weill Medical College of Cornell University where he served as a mentor, administrator and researcher for more than 38 years. He was head and director of clinical training of psychology in psychiatry at the medical college for 25 years.

Clayson was co-founder and charter president of The Association of Professors of Psychology in Medical Schools, the first nationwide organization of its kind in the United States and Canada. He also had been prominent in state and national organizations for psychology professionals and was a consultant at the Memorial Sloan-Kettering Cancer Center and at The Hospital for Special Surgery.

Based on his own research, Clayson wrote extensively on the psychological effects of orthopaedic surgery in adolescents and children.

The legacy he leaves with this professorship mirrors Clayson's lifelong dedication to teaching. He was the first recipient of the Dean's Award for Lifetime Achievement in Teaching at Weill Medical College of Cornell University.

In addition to his many other honors, awards and prizes, Clayson once noted with pleasure that a former student had named his first son after him. In a recent interview, Clayson said: "I always tell my students they are my purpose and my family."

Editor's note: Dr. Clayson had the opportunity to review and enjoy an earlier version of this article a few days before his death.
Medical alumni from the Classes of '41, '46, '51, '56, '61, '66, '71, '76, '81, '86 and '91 gathered together over three fun-filled days, May 10-12, 2001, to catch up on one another's careers and lives, and to reminisce about the "good old days" at the School of Medicine.

Six outstanding alumni/faculty were given special awards. Enjoy a taste of the weekend's highlights on the following pages.

Distinguished Service Award
Robert M. Senior, MD, is Dorothy R. and Hubert C. Moog Professor of Pulmonary Diseases in Medicine and professor of cell biology and physiology at the School of Medicine. He is highly respected as a clinician and teacher and has played an important role in the life of the medical school and its affiliated hospitals. Senior is currently principal investigator of two studies funded by the National Heart, Lung and Blood Institute.

Alumni Achievement Awards
Herbert T. Abelson, MD '66, is the George M. Eisenberg Professor and chairman of pediatrics at the University of Chicago Pritzker School of Medicine and physician-in-chief at University of Chicago Children's Hospital. He has served on several distinguished journals and, in 1997, as the chairman of the American Board of Pediatrics.

Theodore C. Feierabend, MD '51, is a retired medical missionary now living in Madison WI. He is a member of the board of the ecumenical Triangle Community Ministry, which serves an area of public housing and private low-income housing in the city. He has trained physicians in India and Afghanistan, and opened a department of plastic and reconstructive surgery and a burn unit in northern India.

Frank Vellios, MD '46, is retired but continues to serve as a consultant in surgical pathology at St. Joseph's Hospital in Atlanta. He held faculty positions at a number of medical schools and served as editor-in-chief of the American Journal of Clinical Pathology.

Alumni/Faculty Awards
Richard W. Hudgens, MD '56, is professor of psychiatry at the School of Medicine and has served the department in a variety of capacities. He was the first faculty member named Teacher of the Year, an award created by the Class of 1966, and was among those named Clinical Teacher of the Year by the Class of 2001. He has regularly served as reunion chairman for his class.

Alan L. Pearlman, MD '61, is professor of neurology and of cell biology and physiology at the School of Medicine and is also director of the neurology service at St. Louis ConnectCare. He is the coursemaster for the second-year course, Diseases of the Nervous System, and directs the third-year neurology clerkship. Students have repeatedly honored his teaching by bestowing upon him the Distinguished Service Teaching Award, Clinical Teacher of the Year, and Professor of the Year. He regularly serves as his class reunion chairman.
Michael Lewis, MD '76, and class social chair John Milton, MD '76, are all smiles at the welcoming reception.

Dancing the night away, Arthur Schmidt, MD '46, and his wife, Joane.

Dick Hawkins, MD '46, and James Sisk, MD '46, catch up at the reunion banquet.

Good Times

Richard Hudgens, MD '56, and Stanley Smith, MD '56, visit at the welcoming reception.

From left, Walter German, MD '51; Lowell Gess, MD '51, and Taney German, NU '50.
Marvin Levin, M.D., welcomes his classmates to the class dinner.

Joe Moreland, M.D., and Cramer Reed, M.D., both from the Class of 1941, reminisce at their class dinner.

Class of 1951 social chair Marvin Levin, M.D., welcomes his classmates to the class dinner.

From left, Penny George; Philip George, M.D. '66; class social chair Kevin Schaberg, M.D. '66; Tosca Schaberg; Erin Crane; Fay Bisno, and David Bisno, M.D. '66.

Oren Conway, M.D. '71, and his wife, Rose, attend the "Docs Off Duty" program.

Class of 2001 president Andy Josephson, M.D., speaks at the reunion banquet.

"Docs Off Duty" participant Alison Stuebe, M.D. '01, explains how she designed on-line study guides that are now used at the School of Medicine.
Robert Anschuetz, MD '76, shares a memory at the Class of 1976 dinner.

Members from the Class of 1961, from left, John Balfour, MD; Ron Rosenthal, MD, and John Crosson, MD.

J. William Campbell, MD '77, incoming president of WUMCAA, accepts the gavel from outgoing president, Thomas Pohlman, MD '76.

Betty Knoblock, NU '51, and Frank Vellios, MD '46, enjoy a story told at the Class of 1946 dinner.

Capturing memories of his 50th Reunion, George Krietmeyer, MD '51, takes a photo at his class dinner.

Jill Trice, MD '76, speaks at the scientific presentation about lupus and her personal battle with the disease.

From left, Herb Iknayan, MD '56; Sheila Iknayan; Toni Johnson, and Alan Johnson, MD '56, at the welcoming reception.

TRADITION

SHUTTER BUG

APPLAUSE!
Samuel Schechter, MD '41; Norma Bonham, and class social chair Vergil See, MD '41, at the Khorassan Room.

Pankaj Gore, Ann Tilley, Paula Gerber and Chris Combs from the Class of 2001 celebrate at the reunion banquet.

From left Marlene Jessurun; Eric Vaughn, MD '91; Shona Clay, and Carlos Jessurun, MD '91, visit with William A. Peck, MD, dean of the School of Medicine.

Charles Goldman, MD '81, Tom Prater, MD '83, Micki Klearman, MD '81, and Janice Semenovich, MD '81, enjoy hearing from other classmates.

Peggy Gramates, MD '91, Pearl Serota, MD '91, and Harvey Serota, MD & FHS '88, at the Class of 1991 dinner.

Reunion is a family affair for Mandy Doumit; Aziz Doumit, MD '91, and their son, Semser "Sam."


Class Notes

40s

Elmer B. Miller, MD '43, a retired general surgeon, writes that he is "living with my wife, Judy, and our 16-year-old son in the middle of a tract of Carolina forest, where I tend five dogs, five cats, a goat, a donkey, ducks, geese, etc." The Millers live at Pittsboro NC.

Russell D. Shelden, MD '49, is president of the Missouri Senior Golf Association. He lives in Kansas City.

Laura Wexler, MD '71, has been appointed associate dean of student affairs and admissions at the University of Cincinnati College of Medicine, where she has been since 1987. She was formerly chief of cardiology at its affiliated Veterans Affairs Medical Center and interim chief of the division of cardiology at the University of Cincinnati Medical Center.

Charles R. Noble, MD, HS '74, retired from his solo private practice of dermatology on August 31, 2000. He lives in Orlando FL.

Roger Alan Brumback, MD, HS '75, on January 1, 2001, became professor and chairman of the department of pathology at Creighton University School of Medicine and St. Joseph Hospital in Omaha NE.

Al Brock King, HA '76, is president of Memphis Managed Care Corporation.

Sanford P. Sher, MD '76, of Philadelphia has been busy obtaining a state historic marker for Mower General Hospital, which was recently dedicated. Mower, one of the largest and most innovative hospitals during the Civil War, had 3,600 beds and treated more than 20,000 patients from every major battle from Gettysburg until the end of the war.

Scott Greenwood, MD '77, and Pam Freeman, MD '77, live in Orlando FL, where he is president of the Orlando Heart Center and managing partner of a 16-member group, and she practices with Caryn Hasselbring, MD '82. Pam recently was chosen as "Best Rheumatologist in Central Florida" by Orlando Magazine.

Charles Ettelson, MD '78, is serving this year as president of the medical staff at St. Luke's Hospital in Chesterfield MO. He is also chief of the Section of Plastic Surgery at St. Luke's, where he has been in private practice since 1983.

Scott A. Mirowitz, MD '85, began a new position March 1, 2001, as professor and chairman of the department of radiology at the University of Pittsburgh Medical Center.

Clifford V. Harding III, MD, PhD '85, has been named director of the Medical Scientist Training Program at Case Western Reserve University School of Medicine in Cleveland. A professor of pathology and oncology there, Harding has been on the faculty since 1993. His research interests are in immunology and cell biology, and relate to clinical problems in infectious diseases.

50s

Dottie Llewellyn Rodgers, MD '50, has sold her property in Columbia MO, and become a Californian. She is enjoying being able to garden year-round. Her granddaughter, Sarah Schooler, graduated from medical school at the University of Virginia in May.

Godofredo Herzog, MD '57, retired from practice in September 2000 and now lives in Longboat Key FL, where he enjoys beaches, biking and travel. He writes that he is "still married to Eva, and loving it for the past 44 years." The Herzogs have three married children and seven grandchildren who visit frequently. His next project is to write a memoir and perhaps a novel.

60s

Margaret L. Hayes, MD, HS '66, is retired but keeps involved with hospital and medical society affairs in Dayton OH. She chairs the Ethics Committee of the Montgomery County Medical Society. She says, "I do miss delivering babies, but I don't miss insurance companies, etc. I've done some traveling and learned to play bridge. Golf may be next!"

James McCulley, MD '68, chairman of ophthalmology at the University of Texas Southwestern Medical Center, has been named to the board of directors of Reading and Radio Resource, a Dallas organization devoted to meeting the reading needs of people who are visually, physically and learning impaired. McCulley directs the Jean H. & John T. Walter Jr. Center for Research in Age-Related Macular Degeneration and holds the David Bruron Jr. Chair in Ophthalmology.

70s

Scott A. Mirowitz, MD '58, became a new position March 1, 2001, as professor and chairman of the department of radiology at the University of Pittsburgh Medical Center.

Clifford V. Harding III, MD, PhD '85, has been named director of the Medical Scientist Training Program at Case Western Reserve University School of Medicine in Cleveland. A professor of pathology and oncology there, Harding has been on the faculty since 1993. His research interests are in immunology and cell biology, and relate to clinical problems in infectious diseases.

80s

Sharon Mayer Schwartz, OT '95, and husband Steve celebrated daughter Alyssa's Bar Mitzvah in March. Their son, Michael, is a varsity soccer and tennis player in high school and an aspiring cardiologist. They live in Plainview NY.

Nichol M. Trump Lee, MD '93, and husband Gabriel are two of three pediatricians at the Naval Hospital at Naval Air Station in Lemoore CA. They enjoy a busy outpatient practice, with occasional inpatients and about 30 deliveries a month. They have "ample opportunity to participate in the administrative side of military medicine as well." The Lees plan to be there another two years or so and would love to hear from classmates traveling their way.

Charles K. Lee, MD '97, writes that he married "the love of my life," Nakyung Kim, MD, on June 18, 2000, in Chicago, where they live. He recently finished his portion of general surgery and began his plastic surgery fellowship at the University of Chicago. The couple honeymooned in Portugal, Korea and Thailand.

90s

The couple honeymooned in Portugal, Korea and Thailand.
did postgraduate work at Columbia University in New York. She was a nurse and nursing supervisor at Veterans Administration hospitals and clinics for 27 years. She was the widow of Fred Askey and the wife of Howard Ezell, whom she married in 1982. In addition to her husband, she is survived by a son.


Joe R. Utley, MD '60, died in Spartanburg SC, on January 15, 2001, following a long illness. He was 65. A cardiothoracic surgeon, he practiced in California and Kentucky prior to moving to South Carolina in 1983, where he was chief of cardiac surgery at Spartanburg Regional Medical Center until his retirement in 1995. In the early ’60s he served as a flight surgeon in the U.S. Air Force. He founded the Cardiothoracic Research and Education Foundation for furthering knowledge related to cardiopulmonary bypass surgery in 1979. An enthusiastic musician, he played trumpet with the Spartanburg Symphony Orchestra and, with his wife, amassed a collection of rare brass instruments that resides at America’s Shrine to Music Museum in Vermillion SD, where the Utleys established the Joe R. and Joella Utley Institute for Brass Studies. His wife of 44 years, Joella F. Utley, MD '67, a radiation oncologist, survives, along with a son, a daughter and other relatives.

Mary Kay Burgess, DT '69, of St. Louis MO, died of cancer on March 13, 2000. She was 53.

**Faculty**

Viktor Hamburger, PhD, famed biologist and the Edward Mallinckrodt Distinguished University Professor Emeritus in Arts & Sciences, died Tuesday, June 12, 2001, in St. Louis after a short illness. He was 100.

Hamburger was considered a giant in neurobiology, embryology and the study of programmed cell death, and often has been referred to as "the father of neuroembryology." He earned a doctorate from the University of Freiburg in 1925. After completing postdoctoral studies in Germany, he received a Rockefeller Fellowship to study for a year with Frank Lillie at the University of Chicago in 1932. His intended one-year stay in the United States became extended indefinitely when he received word that he was not welcome to return to Freiburg due to Hitler’s “cleansing” of German universities. Hamburger joined the Washington University faculty in 1935 as assistant professor of zoology. Within six years he had advanced to full professor and department chair. He continued to serve as chair until 1966 and was appointed the Edward Mallinckrodt Distinguished University Professor of biology in 1968. He assumed emeritus status in 1969 but maintained an active, well-funded research program until he was well into his 80s.

Hamburger received many honors and accolades, including the National Medal of Science, the Horwitz Prize, the Harrison Award, the Gerard Prize and, most recently, the inaugural Lifetime Achievement Award from the Society for Developmental Biology, conferred June 7, 2000. He also was a member of the National Academy of Sciences and the American Academy of Arts and Sciences. Hamburger was preceded in death by his wife, Martha Fricke Hamburger, in 1965. He is survived by daughters Carola Marte, MD, a physician in New Haven CT, and Doris Sloan, PhD, professor emerita of geology at the University of California, Berkeley, and by four grandchildren, two great-grandchildren and a great-great-grandson.
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**Double Life**

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Alzheimer's on Stage  Members of the St. Louis Black Repertory Company perform “The Eighth Day of the Week,” a play about African-American family members' struggle to care for their mother, who has memory loss and dementia. Sponsored by the School of Medicine and its Alzheimer's Disease Research Center, the Alzheimer's Association of St. Louis, and the Black Rep, the production aimed to increase awareness of the disease in the African-American community and to educate the public about its early warning signs.
Retinal Spots  Age-related macular degeneration (AMD) is often characterized by drusen, spots on the retina. Drusen alone do not usually affect vision; however, in more serious forms of AMD, leakage from abnormal blood vessels can lead to severe vision loss. For more on AMD, please turn to page 8.