In the time before complicated admission procedures and certificates of identity, gaining admittance to medical school lectures was like getting into the theater: You had to have a ticket such as this one. For the story of the School of Medicine's prehistory, see page 18.
Remarkable Achievements

Taking the logical approach to lung transplantation, surgeons save both organs and lives.

The Worm's Turn

A common nematode shows geneticists the way.

Forerunners

The School of Medicine's earliest history established a tradition of cooperation and consolidation.

Newsbriefs

Student Stage

Alumni Report

On the Cover:

Single-lung transplant recipient: Beth Thorne exercising in Forest Park the week of her return to her Florida home. Thorne had been in St. Louis for six months first preparing for, then reconditioning after, her operation.

Photograph by Tom Heine.
Are Cow Antibodies Colic Culprit?

Findings that significant quantities of cow antibodies are present in most human breast milk as well as in milk-based infant formulas suggest that these cow proteins may be a major cause of infant colic, researchers say.

Recent research suggests that proteins in the milk of cows — even gentle Jerseys — may be a cause of colic in infants, whether they are accustomed to formula or mother's milk.

"Until now physicians have been unable to explain why colic seems to occur with equal frequency in breast-fed infants and in formula-fed infants," says principal investigator Anthony Kulczycki Jr., M.D., associate professor of medicine at Washington University School of Medicine. Previously, it had been suggested that colic in breast-fed infants might occur because nursing mothers absorb a protein from their diet and transfer it to their breast milk. But until now, only trace amounts of dietary proteins had been found in human milk. Conversely, the major proteins in cow's milk — caseins, lactoglobulin and lactalbumin — are present in very high concentrations in infant formulas.

A study of 124 breast milk samples from 97 mothers and 25 milk-based formula samples shows that cow immunoglobulin G (IgG) antibodies are often present in microgram per milliliter concentrations in both human breast milk and in commercial infant formulas.

"Although most dietary antigens are destroyed by digestive enzymes, we suspect that the cow IgG antibodies may be more protected from digestion, better absorbed by specialized receptors, or selectively concentrated in human milk," says Kulczycki. "We were surprised to find that levels of cow IgG antibodies were higher in 22 of the mothers' breast milk samples than in one of the commercial cow's milk formulas. Now we have the first logical explanation of why 20 percent of breast-fed infants and 20 percent of formula-fed infants have colic."

Infant colic affects almost one million U.S. infants annually. Colic usually begins after two weeks of age and can last three to four months. The excessive crying associated with infant colic often lasts more than three hours per day and occurs particularly during the evening and night.

"The children are difficult to console and have high-pitched cries and tightened abdominal muscles," says co-investigator Patrick S. Clyne, M.D. Although often regarded as a problem that will spontaneously resolve, colic can be a significant problem and has occasionally been implicated as a trigger of child abuse, adds Clyne, pediatric resident at St. Louis Children's Hospital.

"Our data suggest that two factors are involved in the colic of breast-fed infants — first, whether the mother's milk contains a significant amount of cow IgG antibodies, and second, how the infant reacts to the cow proteins," says Kulczycki.

"We suspect that the reason infant colic may take a week or more to improve, after the breast-feeding mother starts to completely avoid milk and dairy products as recommended, is that cow IgG antibodies are removed from human milk and infant tissues extremely slowly, unlike other dietary proteins," says Clyne.

Schreiber To Head Obstetrics And Gynecology

James R. Schreiber, M.D., has been named professor and head of the Department of Obstetrics and Gynecology at Washington University School of Medicine.

Schreiber's appointment, effective July 1, was announced by William A. Peck, M.D., vice chancellor for medical affairs at Washington University and dean of the School of Medicine. Schreiber will replace H. Marvin Camel, M.D., who has been acting head of the department since Jan. 1, 1990.

"James Schreiber is a fine clinician, researcher and teacher whose administrative talents will provide the Department of Obstetrics and Gynecology with outstanding leadership for years to come," says Peck.

Schreiber comes to Washington University from the University of Chicago, where he has been on faculty since 1982. In addition to his School of Medicine position, he will serve on the staffs of Barnes and Jewish hospitals.
and Regional Medical Center.

Schreiber's clinical interests are in evaluating treatments for infertility — a problem that affects 20 percent of all couples — and developing therapy for recurrent spontaneous abortion. He is currently involved in a prospective comparative study of immunotherapy for recurrent spontaneous abortion. Schreiber says one theory behind recurrent miscarriage is that the mother fails to produce adequate blocking antibodies to shield the placenta from rejection. His study involves injecting the

mother with white blood cells taken from the husband, possibly immunizing her and enabling her to produce blocking antibodies to protect the placenta. The study examines whether this therapy is effective and whether this theory of the etiology of this problem is correct.

James R. Schreiber, M.D.

Edison Foundation To Fund Scholarship

The Harry Edison Foundation has donated $150,000 to the Medical Scientist Training Program (MSTP) at Washington University School of Medicine.

Chancellor William H. Danforth announced the gift, which will be used to establish a scholarship in the name of I. Jerome Flance, M.D., clinical professor of internal medicine at the School of Medicine. "We are truly grateful for the Harry Edison Foundation's vision and for its commitment to educating future physicians and scientists," says Danforth. "Especially, I am pleased at the recognition of a very distinguished physician, Dr. Jerry Flance."

The Flance Scholarship will support a student throughout his or her MSTP training at the School of Medicine. Students in the program receive both M.D. and Ph.D. degrees after completion of six years of study.

"Washington University's MSTP is the best program of its kind in the nation," says William A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine. "It is a veritable wellspring of talented individuals who will make outstanding contributions to medical knowledge in the future. This support from the Edison Foundation will assist us substantially in making a fine program even greater."

Washington University's MSTP, which began in 1968, is the largest MSTP in the United States. The National Institutes of Health has funded 29 such programs nationwide. Directed by Carl Frieden, Ph.D., professor of biochemistry and molecular biophysics, the program here offers outstanding medical students an opportunity to train as academic physicians with a background in basic research.

Since 1974, 148 students have graduated from the program and almost all have gone on to careers in academic or research institutions. Of the 72 students who have completed their residencies, 62 are full-time faculty members. Twenty-three of those individuals are professors or associate professors, 37 are assistant professors and two are instructors.

Flance's association with the School of Medicine spans more than 50 years. He received his undergraduate degree from Washington University in 1931 and his medical degree in 1935. The Flance Visiting Professorship was established in 1976 and is supported by Flance's friends and colleagues to honor his outstanding contributions to teaching.

The funds of the Harry Edison Foundation are used to support education, social services, research and other charitable activities.

W. Thomas Thach, M.D.

Thach Named Director Of IWJ

Thomas Thach, M.D., has been named director of the Irene Walter Johnson Institute of Rehabilitation (IWJ) at Washington University School of Medicine. Thach has been acting director of IWJ since 1989. His appointment was announced by William A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine.

"In Dr. Tom Thach, IWJ will have as its director a leading neurologist and neuroscientist whose clinical and research interests match the mission of this outstanding facility," says Peck. "We are most pleased that he has accepted the appointment."

Thach is professor of anatomy and neurobiology, and of neurology and neurological surgery at the School of Medicine.

Thach joined the School of Medicine faculty as an associate professor in the Department of Anatomy and Neurobiology in 1975 and became a full professor in 1980. Prior to that he served on the faculty at Yale University School of Medicine.
New Test Screens For Prostate Cancer

A simple blood test is the most accurate single method for detecting prostate cancer, according to a study of nearly 2,000 patients reported recently in the *New England Journal of Medicine*.

The test may make it possible to diagnose prostate cancer earlier than ever before, say physicians here. The 10-minute test measures levels in the blood of prostate-specific antigen (PSA), a protein produced only in the prostate gland. Higher-than-normal concentrations of PSA are an indication of prostatic disease. PSA has been used to monitor the progress of prostate cancer treatment, but this is the first large study indicating that it is effective as a screening tool.

Results from the first two years of a five-year study show that the PSA blood test is more accurate than either rectal examination or ultrasound and most effective when used in combination with those techniques, says principal investigator William J. Catalona, M.D., head of urologic surgery at Washington University and Barnes Hospital. When used along with rectal examination — traditionally the gold standard for diagnosing prostate cancer — the test improves detection of the disease, he says. Without the blood test, 30 to 40 percent of prostate cancers in the study sample would have been missed. Prostate cancer is the most common cancer in men over 50 and results in 30,000 deaths each year.

"We hope that the PSA blood test in men will be similar in its impact to the mammogram in women," says Catalona. "We'd like to see all men, beginning at age 50, have their PSA levels checked at least annually as a screening test for prostate cancer. Our study shows that the best way to evaluate a man's prostate is to do a PSA study and a digital rectal examination. If there are abnormalities on either one of those, then further diagnostic tests are indicated."

The *New England Journal of Medicine* article reports results of PSA testing in 1,953 men aged 50 and over. Only 10 percent of the participants had abnormal PSA measurements. Of those with mildly elevated levels, about a fourth had cancer that was usually localized, meaning it was confined to the prostate and therefore curable. In contrast, nearly two-thirds of those with higher PSA levels had prostate cancer, often advanced cases. According to Catalona, the results hold true for an additional 7,000 men who have participated in the study since the *New England Journal* article was submitted.

"These are all men out walking on the street who had no idea that they had prostate cancer, so it's clear, in these patients at least, that prostate cancer was detected earlier than it would have been otherwise," Catalona says. Treatment is more effective and survival rates are higher in patients whose cancer is detected early, he notes. Also, bladder control and sexual function can best be preserved when the disease is caught in its earlier stages.

Catalona and his colleagues measured PSA concentrations in 1,653 healthy volunteers, performing rectal examination and prostatic ultrasound on those who had levels greater than four nanograms per milliliter. Patients with abnormal findings on either of those examinations were biopsied. Results were compared to those of 300 controls, men aged 50 or older who were biopsied because of symptoms or abnormal rectal examination findings.

Ninety-two percent of the 1,653 men enrolled in the study had normal PSA levels. Mildly elevated levels — 4.0 to 9.9 nanograms per milliliter — were detected in 107 (six percent) and markedly increased levels — above 10 nanograms — in 30 (two percent).

Of the men with mildly elevated PSA, 85 were biopsied and 19 (22 percent) had prostate cancer. In the group with markedly elevated PSA levels, 27 were biopsied and 18 (68 percent) had cancer. Overall, 37 of the 112 men who had biopsies (33 percent) had cancer. Men who had elevated PSA levels but negative biopsies were found to have benign enlargement or inflammation of the prostate. In the control group, 72 men (24 percent) had prostate cancer.

Although rectal examination and ultrasound can predict cancer, PSA levels provide the greatest predictive value, Catalona says. "Men who resisted prostate cancer screening because it involved a rectal exam will probably be more willing to have a simple blood test, so the impact of the PSA test on the number of men who have their cancer caught in its earliest stages is potentially very significant."

Among the 37 men in the study who had cancer, rectal examination alone would have missed the cancers in 12 (32 percent). A mildly elevated PSA level was the only suspicious finding for five of the 37 (14 percent), while seven others (19 per-
cent) with elevated PSA levels had normal rectal examinations but abnormal ultrasonounds. When the three tests were considered individually, PSA measurement had the lowest error rate; pairing the tests, PSA combined with rectal examination had the lowest error rate.

“Our results add to the evidence suggesting that rectal examination can no longer be considered the sole or even the most useful means of detecting prostate cancer,” Catalona says. “Although PSA measurement is also an imperfect screening test, it identifies patients who are at high risk and need further evaluation.”

Most men don’t get checked for prostate cancer unless they experience warning symptoms, which usually involve difficulties with urination, he explains. The risk begins at age 50 in the general population, increases dramatically with age, and is greatest in men who have a family history of the disease.

“Unfortunately, using the traditional techniques for diagnosing prostate cancer, almost 7 out of 10 men have cancer that has spread beyond the prostate at the time it’s detected, which may explain the high death rate,” Catalona says. “It’s conceivable that if the PSA blood test were used on a routine basis, the statistics on prostate cancer could be dramatically changed, so that the vast majority of patients would have their cancer picked up early, rather than late.”

**Q:** What has its own scientific symposium, specially commissioned drama, golf tournament and commemorative T-shirt?

**A:** Washington University School of Medicine’s Centennial Celebration, a year-long festival with its peak in October 1991, that will enhance the institution’s visibility in the community, highlight its many contributions to the nation and cement its world prominence as an institution of education and research.

“In terms of celebration, we hope to have something to appeal to everyone” says Glenda K. Wiman, assistant dean for special programs. “We have planned our celebratory events on a scale that reflects Washington University School of Medicine’s stature. We invite all alumni, faculty, students, staff, friends and members of the community to join us in doing honor to this great school’s long history.”

The major events will occur October 9 through 13 and include:

**Wednesday, October 9**
- Tour of St. Louis for out-of-town guests.
- Golf tournament.
- Welcoming reception at the Gateway Arch.

**Thursday, October 10**
- Tour of historical homes and Missouri Botanical Gardens.
- Dinner at the Hyatt-Regency, followed by a choice of either a dedicated musical performance conducted by Richard Hayman at Powell Symphony Hall or the debut of a specially commissioned play at the Edison Theater.

**Friday, October 11**
- Tour of historic Old St. Charles.
- Gala dinner-dance at the Adam’s Mark Hotel.
- Awards presentation. Guest speaker: C. Everett Koop, M.D.

**Saturday, October 12**
- Dedication of Medical Library and Biomedical Communications Center, featuring Daniel Boorstin and other distinguished guests. Tours and reception to follow in the King Faculty Center.

**Sunday, October 13**
- Private day at Six Flags Over Mid-America for faculty, students, employees and their families.
- A spate of related events also has been planned, including a recent night at a Blues hockey game and a dedicated night at a Cardinals baseball game, scheduled for Friday, August 2. Commemorative datebooks featuring details from the school’s first 100 years were mailed to faculty, alumni, donors, board members, students and staff early in January. The annual alumni reunion carried a centennial theme this year when it got underway May 2, and Mallinckrodt Institute of Radiology’s celebration of its 60th anniversary, September 11-14, is a coordinated event.

Members of the 1991 graduating class and their families were feted with a reception on Thursday, May 16, the evening before commencement. A recognition reception for the 100 current employees who’ve worked the longest for the School of Medicine was held June 7. A “birthday dinner” recognized friends of the school for 100 years of support on June 13 at the Ritz Carlton Hotel. Details of commemorative 5k and 10k runs are yet to be announced as this is written.

Oh, and the custom T-shirts? Promised for late spring delivery, they beat this edition of *Outlook* into the hands of the medical school community.
An article in a recent edition of The New York Times reported that “the number of applications for admission to medical school, which declined steadily through most of the 1980s, is up sharply this year.” The article went on to state that the increase was a result of students looking for “safe careers” along with the recruiting efforts of medical colleges.

W. Edwin Dodson, M.D., associate dean for admissions at Washington University School of Medicine is not certain about the “safe careers” motivation, but he says the medical school’s recruiting efforts have been successful — witness a 26 percent increase in applications to the 1991 entering class from the previous year. That increase compares favorably with a national increase in applicants of 14.4 percent.

“We invite outstanding potential applicants to come visit. We communicate with pre-medical advisors in selected undergraduate programs, inviting some of them to come see St. Louis and the school. And a videotape that reflects the views of our students about medical school here has had a good response.” Dodson says. The result has been that almost 4,500 students applied for 122 positions in the class that will enter in the fall. Dodson says that overall, this is the best recruiting year since 1986. Last year, the nation recorded a small increase in the number of applicants from the previous year.

Most importantly, Dodson reports, the increases are centered heavily among students with the highest pre-med grades and Medical College Admissions Test (MCAT) scores. “Twenty-nine percent of all our applicants are in the highest category,” he says. The average student either accepted or on the waiting list posted an undergraduate grade point average of 3.74 out of a possible 4.0. “This is one of the best-qualified groups we have ever seen,” Dodson says.

He is not convinced that the upswing is attributable to students seeking “safe” professions in the face of recession and uncertain economics; his information shows that 53 percent of all medical students made the decision to go to medical school during or before high school. “Our trends are very long,” Dodson explains.

On the anonymous questionnaire filled out by 98 percent of all medical students on their first day, the two most common reasons given for attending are a desire to be of help or to do relevant research and an appreciation of the intellectual challenge. Dead last on the list is financial incentive. Speaking both as associate dean and as a professor of pediatrics and neurology, Dodson says, “that’s very encouraging for the future of medicine. We’re seeing good scores, good grades and good motives.”

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Associate dean for admissions W. Edwin Dodson, M.D., dined with pre-med advisors Jane Sharaf of Princeton and Kathleen Parson of Macalester College on their recent visit to St. Louis and the School of Medicine.

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Learning To Fish

Sparking in his native Spanish, Gustavo Sequeira, M.D. delivers a Nicaraguan idiom that translates roughly to mean: “We don’t want our fish fried and served on a plate. We must learn how to fish.” Though the subject of his three-week fellowship here — diagnostic echocardiography — is more complex than the piscatorial arts, the analogy is still apt: Sequeira, a professor of medicine and cardiology at the School of Medicine in Leon, Nicaragua, will go home trained to use a helpful technology and prepared to instruct others in its use. Symbolically, he will have learned to fish.
"By coming here to train, Latin American physicians learn the intricacies of echocardiography that can’t be found in books, even if those books were available in Spanish," says Julio E. Perez, M.D., associate professor of medicine and medical director of cardiac diagnostic ultrasound at Barnes Hospital. Perez, himself the author of a textbook on the subject (as yet untranslated), is the force behind the School of Medicine’s International Preceptorship in Echocardiography. Sequeira, who speaks no English, is the program’s third student.

Instruction delivered here will be of particular value to Sequeira in Nicaragua, a country struggling to redefine itself after 11 years of war. Nutritional deficiencies affect many Nicaraguans, access to health care is limited, and the average life span is shorter than in the United States. One of the most difficult health problems facing the country results from rheumatic fever that repeatedly afflicts many young Latin Americans, causing heart disease that eventually leads to valvular failure. Perez says, "A 25-year-old’s valvular heart disease in Latin America resembles what we might see in this country in those 65 or 70 years old." The microorganism responsible has been largely controlled by penicillin treatment strategies in this country since the 1950s.

Tragically, such early valve disease is often seen in Latin American women of child-bearing age. But echocardiography with Doppler — a noninvasive ultrasound technique — is ideal for diagnosing and assessing the severity of the problem, Perez says. Effective but not overwhelmingly complex, it is relatively inexpensive to set up and operate. "In this country, coronary artery disease is an important cause of disability and death, requiring catheterization for accurate diagnosis. A cath lab requires nursing and technical personnel, and it must be supported by a surgical backup," Perez says. Doppler echocardiography can be set up for as little as $50,000, compared to the $1 to $2 million required for a cardiac catheterization lab.

Funds to train Latin American physicians — the first two fellows were from Puerto Rico and the Dominican Republic — are generated by Perez. With the endorsement of Burton E. Sobel, M.D., professor of medicine and director of the cardiovascular division, the money Perez generates by training technicians for equipment manufacturers in the Midwest goes in part to support the international program.

"Training one physician per year, obviously we won’t make much of a dent," says Perez, who hopes to expand his work as financing becomes available. The Inter-American Society of Cardiology has endorsed the program and assists with the identification of candidates for the preceptorship in different countries "to avoid favoritism," Perez says.

The money Perez earmarks pays for round-trip airfare and a room in the Olin Residence Hall. Board is the visiting physician’s responsibility during the instruction period. Perez, a native of Puerto Rico who has been on the Washington University faculty for 13 years, conducts the tutorial in Spanish and includes his visitor in the 20 to 40 echocardiography exams performed here each day. "This polishes my Spanish and keeps me linked to 300 million people. But more, it is an opportunity for me to give back some of what I have learned," Perez says.

Sequeira, who oversees the only Doppler echocardiography machine in all of Nicaragua (a surplus unit donated by Barnes Hospital via Perez), will return to Leon, the country’s second-largest city, to handle referrals from throughout the nation’s 3 million inhabitants. Impressed with the technology he has seen in the United States, he says he hopes to bring a small part of it to bear on health matters in Nicaragua. After 35 years as a cardiologist there, improving the health of his people remains his greatest concern.

Vocally grateful for the opportunity to hone his skills here — to learn to "fish," so to speak — Sequeira takes back with him a positive opinion of North Americans: "They are not materialistic, but rather humanistic and interested in helping us solve our problems," he says.
ix months ago, 28-year-old Beth Thorne’s life depended on massive dosages of an experimental drug that, had she been paying for it, would have cost her about $2,800 a day.

A pulmonary hypertension patient, she needed continuous infusion of the drug, prostacycline, to ease the strain on her overworked heart. For two-and-a-half years she wore a drug delivery device she called “Peter the Pump;” as soon as one syringe of medication was empty, Thorne replaced it with another. One time she dropped her syringe and didn’t realize the tip had snapped until just before she fainted, as pulmonary hypertension patients frequently do. Lapsing in and out of consciousness, knowing she had only 90 seconds to live, she crawled across the room, grabbed a new syringe and hooked herself up.

Thorne was fortunate a second time: on January 25 — her birthday — she underwent a new procedure called a single-lung transplant, in which she received a healthy lung that, by functioning normally, has taken the burden off her heart and allowed it to recover. “It’s the best birthday present in the world,” Thorne says. “I’m almost normal now.”

The operation was performed by a team headed by Joel Cooper, M.D., professor of surgery, head of general thoracic surgery and director of Washington University Medical Center’s lung transplantation program. According to Cooper, the single-lung transplant represents the most encouraging advance in almost a decade for pulmonary hypertension.

The single-lung transplant represents the most encouraging advance in almost a decade for pulmonary hypertension patients.

patients like Thorne, who previously have had to pin their hopes on the possibility, however remote, of getting a heart-lung transplant before they die.

The race with death Beth Thorne won shortly before her transplant vividly illustrates the tenuous and sometimes desperate existence of patients with pulmonary hypertension. It’s a disease of young people, generally, and of women more than men. Patients first notice weakness, fatigue and shortness of breath. Thorne, who had always been healthy, initially thought she was out of shape and needed more activity. But when she was unable to complete her self-imposed exercise program, she went to the doctor believing she had asthma. Symptoms progress gradually until patients can’t really do anything: They have difficulty climbing stairs, they can’t walk quickly, they may need wheelchairs or oxygen tanks. Thorne — a telecommunications manager accustomed to jogging, jet skiing, riding her bike and boating — found herself housebound.

Very little is known about the prevalence of this uncommon disease, the cause of which remains a mystery. But the course is clear. The blood vessels of the lung — the pulmonary arteries — become increasingly narrow and fixed, forcing the heart to work harder and harder to pump blood through the lungs. Eventually, the overtaxed heart begins to fail. Any increase in activity demands a corresponding increase in oxygen, meaning the already over-exerted heart must pump more blood, a strain that puts the patient at risk of sudden death. And many do die; the average life expectancy is 2.8 years after the condition is discovered.

For years, there was no hope for pulmonary hypertension patients. Then in
1981, surgeons at Stanford University reported success with the combined heart-lung transplant for patients who had both failing lungs and a failing heart. The procedure became standard for patients with pulmonary hypertension as well as those with an even rarer condition called Eisenmenger's Syndrome, in which a hole in the heart leads to the same irreversible narrowing of the pulmonary arteries.

The combined operation is still used, but the single-lung transplant is catching on, says Cooper. The medical center's transplant program — conducted at Barnes and St. Louis Children's hospitals — has the largest and most successful experience with the procedure, which it began performing in the fall of 1989. Of the first 10 patients to receive single lungs — two at Children's Hospital and eight at Barnes — all have survived, regained normal cardiac function and resumed normal lives.

"It seemed logical that if you just put in a lung and basically correct the plumbing, the heart will not have to pump under such load and will recover," Cooper says of the idea to substitute the single-lung operation for the heart-lung transplant. "And that's exactly what happens. When you take one of these patients with an absolutely terrible heart and put in just one lung, it takes all the blood flow with normal pressures, and the heart immediately shows marked improvement and then over a period of weeks and months gradually improves further."

One of the advantages of switching to the single-lung transplant is that it allows not one but three people to receive donated organs, and faster than they would have previously. Cooper points out. "These people were waiting years for heart-lungs, often dying while waiting. Heart-lungs are difficult to come by because the heart-lung is much more complicated and not as successful as the heart transplant," he explains. "By using one lung, the wait is much much shorter, we can use each of the lungs and the heart for three different recipients and increase the number of transplants."

Because the benefits of this new procedure are so great and the success rate of lung transplants has improved dramatically in recent years, Cooper feels that many patients previously considered for heart-lung transplant would be better served by a lung transplant.

"We initially employed the combined heart-lung procedure as the only method of replacing both lungs in certain patients with end-stage lung disease," he wrote in an editorial for the European journal Transplant International. "We soon recognized that the heart was being replaced not out of physiologic necessity but for technical expediency."

His solution was to develop the en bloc double-lung transplant, a method for removing donor lungs without jeopardizing the donor heart, allowing it to be used for a cardiac transplant. In 1987, he reported success in six of seven patients who received the double-lung transplant; all six are still in excellent health and have no significant deterioration in lung function.

Since that time, Cooper has refined the procedure to reduce airway complication and to make it less complex and thus more easily adopted by other transplant centers. The technique, now called the bilateral lung transplant, has proven highly successful in patients with cystic fibrosis and emphysema. Both lungs are transplanted, but each is replaced as a separate unit, eliminating the need to shut down the heart and use a cardiopulmonary bypass.

Cooper's team now performs both the bilateral and single-lung procedures for patients with emphysema. For years, these patients have been turned down for lung transplants because of early unsuccessful efforts, but with improvements in lung preservation and immunosuppression, emphysema has become the most common indication for transplant, Cooper says. At Washington University Medical Center, the bilateral operation is reserved primarily for patients under age 50, and the single-lung procedure has yielded excellent results in older patients with this chronic lung disease.

The first-year results of the bilateral lung transplant are impressive. Of 21 recipients, 19 — 91 percent — are alive and well. "The goal of developing a safe and effective procedure for replacement of both lungs without the heart has now, in our opinion, been achieved," Cooper wrote in the editorial. The success of the bilateral lung procedure is similar to that of the single-lung transplant, for which he reported 28 recipients in the first year and an operative survival of 96 percent.

The achievement those records reflect is particularly gratifying, considering lung transplantation's historically gloomy record. Single-lung transplantation began in the early 1960s and was dropped as a viable idea 20 years and 45 failed transplants later. In the late 1970s, the immunosuppressant cyclosporine became
Group support is provided for those waiting to receive lung transplants and those in rehabilitation following successful surgery.

available, solving some of the healing problems caused by the corticosteroids that were used for immunosuppression in early cases. Cyclosporine and improved techniques allowed surgeons to begin accumulating successes.

In November 1983, Cooper — then at the University of Toronto — performed the world's first successful human lung transplant, replacing the right lung of a 60-year-old patient suffering from idiopathic pulmonary fibrosis. Three years later, he and his surgical team successfully completed a double-lung transplant in a 43-year-old emphysema patient.

Cooper joined the Washington University School of Medicine faculty in 1988 and since then has established at the medical center one of the most successful lung transplantation programs in the world and one of the few thoracic training centers in this country. The program here has an initial success rate of more than 90 percent, and, according to the international registry that Cooper maintains, lungs are being transplanted with a one-year success rate of 68 percent worldwide. He fully expects those numbers to improve even further.

"The goal of developing a safe and effective procedure for replacement of both lungs without the heart has now, in our opinion, been achieved."

As exciting as it is to have more and more surgical success, to get more people out of hospital and restored to health, it becomes correspondingly more frustrating that a certain percentage of people who have any kind of transplantation are going to die of rejection or complications over a period of years," he says. "There's an inevitable attrition along the way."

Rejection and infection are the banes of all transplantation, he says. "If you increase the immunosuppressants to try to reduce rejection, you increase greatly the infectious complications because the body's defenses are weakened. If you try to keep infection down by reducing your anti-rejection drugs, then rejection becomes the major problem."

Better and more precise drugs are needed, and a number of new immunosuppressants are "in the pipeline," Cooper says. He and other transplant surgeons are optimistic that better solutions to the problems of rejection and infection are coming soon. He hopes also that his current patients will benefit from the ever-increasing knowledge of molecular biology and immunology.
Toward that end, tissue is removed from the deteriorated lungs of patients who receive single-lung transplants here so that molecular biologists can determine the sequence of events that leads to narrowing of the pulmonary arteries. In addition, Cooper works with virologists testing drugs designed to reduce the incidence of cytomegalovirus infections, common among transplant patients. And he and his associates conduct long-term follow-up studies of all transplant patients to monitor heart function, watching for any signs that the disease necessitated the transplant is returning to attack the new lung.

Besides rejection and infection, another crippling problem transplant patients face is cost: They incur sizeable medical and hospitalization bills. If necessary, Cooper helps his patients collect from their insurance companies.

The university and hospital get paid in about 80 percent of the cases, he says. He has no quarrel with companies that have specific exclusion policies against transplantation. "We fight those that attempt to deny coverage on the basis that these procedures are considered experimental or investigational. And we win."

His argument is that lung transplantation is neither investigational nor experimental. "When you've demonstrated that lung transplantation can be successful, and when you've applied it only when there is no alternative — the patient is dying, all other possibilities have been exhausted — then that is not an experiment," he says. "That is the best treatment you have to offer, even though it's risky, dangerous and uncertain. Under those circumstances, the alternative is death.

"Lung transplantation is logical. It's based on solid scientific background, and on top of that, it works, as we've shown since 1983," he continues. "The number of times it works, the risks involved, are almost irrelevant when it is being used as the only alternative. We have a good success rate. But even if we didn't, it's the only choice."

While in St. Louis, most of Cooper's patients stay nearby at "Transplant Village," otherwise known as Towne House Apartments, on Lindell Boulevard. The complex has no formal arrangement with the medical center but has accommodated the temporary housing needs of transplant patients by waiving any lease requirement for its furnished apartments and making its party room available for monthly luncheons and weekly support group meetings. For the patients, who must relocate to undergo rehabilitation, the village is a godsend.

Rehabilitation is one key to the success of the medical center's program. Most lung transplant patients, particularly those with emphysema and cystic fibrosis, are "conditioned" before their operation. "We work them very hard beforehand to get them built up, and we get them nutritionally in good shape," Cooper explains. "You can gradually train up their muscles, which haven't been used for a long time because they're so oxygen-dependent. Exercise is conducted with continuous monitoring of the patients' pulses and the oxygen levels in their blood."

Patients with pulmonary hypertension or Eisenmenger's syndrome, however, receive no pre-operative training. "These people can't do that. They can't exercise," he says. "We tell these people, 'Just stay quiet,' because if they start exercising, their hearts can't increase the output and they'll pass out." After the transplant, they — like all of the other transplant patients — start by walking, then progress to stair-climbing, bicycling and exercising on a treadmill before beginning to jog on a track.

His patients use the track at Irene Walter Johnson Institute of Rehabilitation, but all other training is conducted in a facility built by Barnes for its transplant patients. On any given day, it's not uncommon to find eight or 10 transplant patients there — some "conditioning," oxygen tank and all, before their operations and others who already have new lungs and are in post-operative training.

"The whole business of rehabilitating these patients — the ability to take people with poorly functioning lungs and build them up and often double their performance, which then shortens their hospital stay and improves their chance of getting through the transplant — is a message for people with end-stage lung disease who may not need a transplant. That is, look what you can actually accomplish if you put your mind to it and you're motivated," Cooper says.

"But of course it's the transplant that motivates them," he adds. "When it's a requirement and you're looking forward to being returned to normal, then the team and you and your doctor all are motivated, and you can accomplish remarkable things."

And Cooper's patients do go on to make remarkable achievements. Ann Harrison, the recipient of the world's first double-lung transplant, in April ran the final leg of a 400-meter relay to finish third at the annual Transplant Games in Toronto. Four years ago, Kathy Urish became the third person to receive a double-lung transplant. Last summer, she climbed Pike's Peak. Beth Thorne, who recently completed her rehabilitation in St. Louis, still has mountains to climb. For now, though, she's content to be home and back at work in Clearwater, Fla., leading a normal life once again. She's resumed the recreational activities she had to forsake two-and-a-half years ago, and in December will achieve her dream, to ski the slopes at Vail.

Cooper, who telephones all of his patients on their transplant anniversaries, marvels at their recoveries. "It's miraculous. Even after all the years, you don't get over it."
Under a microscope, several *Caenorhabditis elegans* lie together, each transparent body curled tightly in its individual egg. One worm squirms restlessly. Others make exploratory nudges. When one finally breaks through its shell, it moves halfway out, then backs up. The next few seconds it spends snaking back and over itself. After a few half-starts, the worm leaves the shell entirely and slithers past its still-captive siblings.

Like the first worm out of its shell, research involving *C. elegans* — a tiny, common nematode — finally seems to be coming into the light. The journey has been marked by relentless work, a few false starts and remarkable cooperation among the 500 researchers worldwide who see the worm as a means to understanding fundamental issues of biology and genetics.

Many believe the best is yet to come. In just two years, Robert H. Waterston, M.D., Ph.D., professor of genetics and acting chairman of the department, and Alan Coulson and John Sulston at the Medical Research Council (MRC) laboratory of Molecular Biology in Cambridge, England, expect to complete work on a physical map of genetic information for *C. elegans* — a set of landmarks for steering researchers to points of interest. Within 10 years, they hope to finish an even more ambitious project: sequencing the nucleotides that make up all of the worm’s genes. (A nucleotide is the smallest bit of chemical information in a gene.)

The *C. elegans* mapping project is more complicated than any done previously because, as an animal, *C. elegans* is a much more complicated organism than yeast or bacteria, the only other organisms fully mapped. And in fundamental ways, the *C. elegans* mapping project is especially important, providing fuel for an ongoing effort to map and sequence human DNA.

The project also offers immediate benefits to researchers who use the worm in their work. The mapping effort provided these scientists with directions to find the genes they want to clone and investigate. “The map tells us where to look, in a very narrow region,” says Waterston. “So people are cloning genes using the physical map all the time now. They’ve seen how useful the physical map has been in the nematode. That’s generated more enthusiasm for a physical map of humans,” he says. A physical map of the complete human genetic code is an initial goal of the human genome initiative. Recently begun officially at four research centers, including Washington University, the initiative is among the largest challenges ever undertaken by biological science.

However, information gleaned in the two projects is not interchangeable.

“Mapping is inherently an isolated activity,” says Waterston. “The map of Europe doesn’t tell you anything about the United States, and the map of *C. elegans* doesn’t tell you anything about the map of humans. But the map-making technologies are transferable.”

Just as the mapmakers of Renaissance Europe honed their skills on maps of England and the Mediterranean before facing the task of charting the New Continent, so have researchers today learned methods in mapping *C. elegans* that are being applied to the human genome project.
C. elegans is a harmless nematode, but it belongs to a group of organisms that includes such parasites as the hookworm and the guinea worm. Small, measuring only about a millimeter in length, the worms are commonly found in dirt, where they feed on microorganisms. They are seldom noticed, except by researchers, because most people don’t ever see them. In addition to being small, they have transparent skin.

That transparency is one of the characteristics that makes the worm so attractive to science. Under the microscope, biological processes are visible with no harm to the animal — a big plus for geneticists who breed subsequent generations from mutants they can identify simply by looking.

Timothy Schedl, Ph.D., assistant professor of genetics, studies how C. elegans germ cells develop into sperm or eggs. “Early in embryonic development, the cells that will eventually form the sperm and the eggs (germ cells) are set aside from the somatic cells that form all of the other tissue,” Schedl explains. During larval development, the germ cells proliferate and differentiate into sperm and eggs. Like all other cells in C. elegans, germ cells are visible under microscopy. That lets Schedl observe the development of each part of the organism over time. He says, “In our work, we examine the germ cells in mutant individuals to deduce what the normal function of the mutated gene is.”

Waterston, in his research involving muscle function, can peer through the worm’s skin to see evidence of mutations that affect muscle tissue. “It turns out that normal muscle has a particular pattern to it — it appears striped,” he says. Most of the mutations Waterston looks for don’t have the telltale stripes, making them easy to locate.

Researchers also like C. elegans because it is relatively uncomplicated. Only 959 cells make up the entire adult animal. The worms are also easy to care for and propagate. They have a life cycle of about three days, during which a single worm can produce 300 progeny. They feed on bacteria and can exist comfortably at room temperature, and they can be frozen without harm — a characteristic that enables scientists to store mutant worm strains for future research without having to worry about feeding or breeding them.

C. elegans displays its convenient transparency. This animal, in the fourth larval stage, will soon molt into a sexually mature adult. Passage from birth to adulthood requires about 40 hours. The animal’s head is the blunter of the two ends, and the bright dots are individual cell nuclei.
In much the way that the genetic map of C. elegans is pieced together, this image of a complete worm is a composite of several photomicrographs. Individual cells are visible in this adult hermaphrodite.

Maphrodites and as males. Males can be bred with hermaphrodites, but researchers often prefer to propagate only hermaphrodites because their offspring breed true. Scientists working with hermaphrodites therefore can more easily analyze changes from one generation to the next.

Because C. elegans is such an attractive research animal, scientists from many different fields use it in their studies. Its simple nature offers a chance to understand the whole organism instead of concentrating on just a single aspect. "That's why some people go into biology in the first place -- to look at an entire organism, not just one or two cells out of context," says Martin Chalfie, Ph.D., of Columbia University. Chalfie uses C. elegans in his studies of neural development.

Mapping The Possibilities

In research conducted during the late '70s and early '80s, John Sulston laid the groundwork for much of today's investigation. From a painstaking study of every cell division in C. elegans, Sulston pieced together a lineage map for the nematode that shows the development and migration of each cell in the worm's body. From there, he and his colleague Alan Coulson set out to construct a physical map of the worm's genetic information.

Having heard of the early stages of the mapping project, Waterston took a sabbatical from Washington University six years ago to visit Sulston and Coulson in Cambridge. "I've been interested in the map since its inception," Waterston says. His interest was fueled partly by watching, for many years, the progress of his medical school colleague Maynard Olson, Ph.D., in the development of a similar map for yeast.

Waterston also had reached a point in his own work on muscle function in C. elegans from which he could go no further without more genetic information. "There was just no ready way of starting the molecular analysis on those genes without the map," he says. And so he returned to St. Louis to set up a collaborating laboratory for the C. elegans mapping project. The two labs now are in regular communication via fax, telephone and electronic mail.

Both labs make their knowledge available to the world research community via a database that shows an up-to-date physical map. Researchers access this information from their computers' modems. And a new database under development will display not only the physical map but also much of the other information available about the worm.

"It's a great catalog of information," says Waterston. "Instead of having to look through all the articles, it's right in front of you, in a systematic display."

A Thousand Puzzles

Mapping the 100,000,000 nucleotides that make up the worm's genetic information has been a huge undertaking. One of the first steps was to break down the project into manageable pieces.

In the first phase, Sulston and Coulson cleaved the worm's DNA into fragments of about 40,000 nucleotides each. Then they used the best means of cloning available, a technique that involved bacteria as a host to make copies of the DNA. But that method offered only limited success. "It turns out that a fair fraction of the nematode's DNA won't amplify in bacteria," says Waterston. At the end of the first phase, there were still holes in the map.

The second phase involved a new process of cloning: the Yeast Artificial Chromosome (YAC) method. "We didn't originate it, but because we were down the hall from Maynard Olson's lab..."
where YAC technology was developed, we were among the first to exploit it,'" says Waterston.

Even breaking down the project into more manageable pieces is not without difficulty, Waterston notes. "What you start with are big, chromosome-sized pieces of DNA," he explains. "There are about 20 million base pairs in each piece, and that's too many to work with. But when you break them up, you lose all the positional information. You don't know where the pieces came from. The challenge is to put these pieces back together in the order that represents the chromosome," he says.

"The analogy is frequently made to doing a puzzle," Waterston says, "but the trouble with that is that if you take a puzzle and jumble the pieces, you know that each piece is there only once. In this case, it's more like mixing up a million puzzles, then trying to take out the 1,000 pieces that you want for one puzzle."

Of course, the bigger the pieces are, the easier it is to put them together correctly. And the YAC method offered researchers pieces of information almost 10 times bigger than what they'd had before.

Waterston hopes that the YAC method and input from other researchers will allow him and his colleagues to complete the map without holes this time. If it doesn't work, he's not sure exactly what the next strategy might be. Right now, there simply are no alternative methods of cloning.

Worms Aid Medical Science

As research using C. elegans spreads into so many fields, it becomes clear that much of what is known about the worm has practical applications for human health. By better understanding the worm, we may eventually learn more about human problems, including degenerative nerve disease and muscle disorders. C. elegans might even shed light on reproductive biology — research on the nematode is yielding insight into methods of cell division. These applications are possible because, in basic ways, C. elegans is similar to all other living organisms, including humans.

"The biology is just not as different as people often think," says Waterston. "We already know that genes of C. elegans are related to mammalian genes. The genes used to make muscle in the nematode are very similar to the genes used to make muscle in humans. Humans might have more copies of the genes, but the sequence of nucleotides is astonishingly similar."

Researchers at Harvard recently discovered a mutation in humans involving the myosin protein of the heart muscle. To study the problem in depth in humans would require removing the heart. "Because you can't do such experiments in humans, you can't show that this mutation is responsible for disease," Waterston says. What he has been able to do, though, is to see how the same mutation affects myosin in nematodes, opening a window on the fundamental processes involved.

Chalfie, in his research on neural degeneration, believes there are similarities in nerve function as well. It's too early to tell how closely nematode mutations affecting touch sensitivity resemble human disorders, but Chalfie and his colleagues believe their research on worms will form the basis of a model for human diseases.

Some take such research a step further. Jonathan Hodgkin, senior staff scientist at the MRC Laboratory of Molecular Biology, suggested in a recent issue of Nature that such nematode research "could also provide a model system for the rapid testing of drugs that might delay or prevent neuronal degeneration."

Scientists working on more general issues compare the nematode to humans, too. Schedl is interested in two aspects of germ cell development that are common to all animals that reproduce sexually. He hopes that by looking at C. elegans he will discover how the determination is made concerning whether a germ cell will become sperm or ovum. A second aspect of his research examines how germ cells decide whether to undergo meiosis or continue to proliferate.

Robert H. Waterston, M.D., Ph.D.

To do this, he isolates mutations that interrupt the normal processes. "These mutations reveal the genes that control germ cell development," Schedl says, adding that some aspects of germ cell development are fundamentally the same from one species to the next, even if there are specific differences.

"Many biological processes and cell types may have arisen early in the evolution of multicellular organisms. The evolutionary process has built upon that early form," he says. Accordingly, C. elegans might hold in its tiny body the keys to unlocking many of the secrets of human development, and a greater understanding of the worm's heritage will illuminate our own genetics. ■
FORERUNNERS

The Earliest History: McDowell's College and Pope's College

by Paul Anderson and Marion Hunt

Charles A. Pope (1818-1870), a leading surgeon of his day.

Joseph Nash McDowell (1805-1868), anatomist and surgeon.
One hundred and fifty years ago, physicians were badly needed but scarce on the American frontier. The celebrated Gateway to the West, St. Louis was a natural location for training doctors and home to the first two medical colleges west of the Mississippi River. Known popularly by the names of their most famous early deans (Charles A. Pope and Joseph Nash McDowell), the two institutions were the forerunners of today's Washington University School of Medicine.

The actual event celebrated in this centennial year is the naming of old Pope's college, formally the St. Louis Medical College, as the medical department of Washington University. Eight years later, in 1899, the faculty of McDowell's college, formally Missouri Medical College, agreed to bury a long rivalry and combine its resources with the university's.

The story began in 1840, when the backers of a newly established Episcopal institution in the city, Kemper College, invited the surgeon and anatomist Joseph Nash McDowell to head a medical department. A Kentucky native, McDowell had distinguished himself in years of teaching and medical practice in Cincinnati. In his inaugural speech, McDowell hailed the importance of the city's location, proclaiming; "We believe the destiny of St. Louis in medicine is not to be equalled by any position in Western America." The Kemper Medical College was built on a little hill overlooking a mill pond, just south of town, near where the Ralston Purina Company's headquarters now stands.

Kemper College did not survive as an undergraduate institution and ceased instruction in 1845. McDowell, however, secured an affiliation with the University of Missouri, and he and his colleagues continued to teach medical students. More importantly, the dean raised money for his own building, which he completed alongside the Kemper hall in 1850. It was a bizarre structure, dominated by an octagon-shaped tower that included battlements and was stocked with small arms to ward off intruders. The affiliation with the state university lasted until 1857, when McDowell decided to operate independently under the name Missouri Medical College.

The Pope's college tradition began under the auspices of still another institution of higher learning. On the north side of town, at Washington Avenue and 10th Street, St. Louis University laid plans to found a medical school as early as 1836. Faculty were named, but there was no place for them to give lectures. In 1842, Dean James Vance Prather donated his house near the campus to the school and authorized the construction of a small hall the following year.

In 1844, the surgeon Charles A. Pope joined St. Louis University, and four years later he became dean. He had studied at European universities and brought with him knowledge of the latest techniques. With the financial backing of his father-in-law, the wealthy banker and real estate baron John O'Fallon, Pope built a medical school building, a graceful neoclassical structure on the south side at 7th Street and Clark Avenue, that opened in 1849. Two years later the building was more than doubled in size with the addition of a wing to house the library, the medical museum and clinics known as the "O'Fallon Dispensary," a designation that lasted into the Washington University years.

Prather, Pope and their colleagues wanted autonomy from St. Louis University and saw to it that their medical school was governed from the start by a nonsectarian board of trustees headed by the Unitarian minister William Greenleaf Eliot (who was later to found Washington University). This arrangement, however, did not withstand a period of intense anti-Catholic sentiment in St. Louis in the early 1850s, fanned at times by the oratory of none other than Joseph Nash McDowell, who was notoriously envious of Pope. In 1855, the school's faculty and trustees decided that it was prudent to separate fully from St. Louis University and received an independent charter from the state as St. Louis Medical College.

Public opinion and public oratory counted so much in medical education of the times because, in fact, there was more than a little show business to the curriculum. Most students enrolled with no formal education but some practical experience from apprenticeships to physicians in their home communities. Matriculation at medical schools in St. Louis and other cities entailed perfumatory registration and the purchase of tickets to each professor's course. That entitled students to hear the great McDowell — or the great Pope — hold forth, much as they might have heard P. T. Barnum or some other illustrious showman of the times. The circus analogy can be extended further, because tickets also provided admission to the
The Civil War

As was the case for much of the business and professional elite of St. Louis in 1861, the faculty of both medical schools included people who identified with the Confederacy. McDowell even left the city to join the Southern cause. His departure led to the cancellation of all courses at Missouri Medical College, despite attempts by John T. Hodgen, an anatomist and surgeon on the faculty, to continue instruction. Matters took a dramatic turn when General John C. Fremont, commander of Federal troops in the city, declared martial law and confiscated the property of leading rebels. The army converted McDowell’s college first into a barracks, then into a prison for captured Confederates.

The faculty of St. Louis Medical College remained loyal to the Union cause, and the school continued instruction during the war. The conflict was undoubtedly a source of particular grief to Pope, a native of Alabama, who distinguished himself in tending the wounded of both sides who were brought to St. Louis. At the war’s close, he resigned his chair and moved to Paris but retained ownership of the college building. He was replaced as dean by Hodgen, who had joined the faculty after leaving the suspended Missouri Medical College in 1862.

McDowell returned to St. Louis after the war and attempted to reopen his college. He found his building nearly in ruins, emptied of its teaching apparatus, museum and library. Where once there had been gardens on the grounds gallows stood. After considerable effort and expense, a faculty was reassembled and the building was refitted with equipment. The task, however, proved too difficult for McDowell. Early in 1868, before instruction resumed, he resigned the deanship in favor of one of his sons.
In September of that same year, Joseph Nash McDowell died.

In 1869, the program of St. Louis Medical College was almost as severely devastated when fire broke out in its building, destroying the expanded east wing and center section. Only the original structure was salvaged. Pope was called home from Paris to inspect the damage in 1870. His colleagues put as brave a face as possible on the situation and warmly feted their old leader. In all likelihood, however, the visit was a sad one for Pope and may have been a contributing factor when he committed suicide not long after his return to Paris.

Both colleges grappled with the same dilemma: How could the faculties continue to teach in damaged, outdated buildings that were, furthermore, not directly controlled by the respective institutions? The problem was resolved in different ways. At Missouri Medical College, Drake McDowell was ousted from his deanship and resigned his chair. That meant, of course, that the college had to move. After a desperate search, the institution rented quarters in an office building at Sixth and Elm Streets, literally around the corner from Pope's college. Instruction began there in 1870. Another tenant of the building was St. Luke's Hospital, but the hospital relocated not long thereafter. [In those years, medical schools and hospitals were still uneasy partners.]

Formal medical education at the turn of the century was based on rote memorization, with material presented on the large display cards depicted in this scene of a lecture hall.

St. Louis Medical College chose to remain in its old building. To this end, the faculty and its backers organized a special association, the Medical Fund Society, to raise money for the purchase of the structure from the Pope estate. Once this mission had been accomplished, the society continued its good work in support of the college, helping it to renovate and expand its facilities, including a new building nearby for the O'Fallon Dispensary.

Reform

By the 1870s, leading physicians were increasingly aware that American medical education needed reform. New scientific and clinical knowledge was rendering the old academic formula of rote memorization obsolete. Many St. Louis doctors with close ties to German universities knew of innovations there that included intensive laboratory training and progressive clinical instruction in hospitals, culminating in formal internships.

In 1873, Missouri Medical College moved again, this time to new quarters at Lucas and 23rd Streets that included facilities for scientific laboratory training as well as lectures. A distinct advantage of the location was its proximity to St. John's Hospital, operated by the Sisters of Mercy and situated directly behind the school. Association with St. John's did not lead immediately to full adoption of the German concept of medical education, but it did induce a teaching hospital affiliation that lasted until 1903. Dean during most of those years was Paul Gervais Robinson, whose affable personality stood in marked contrast to the elder McDowell's.

St. Louis Medical College did not boast an adjacent teaching hospital, but by 1868 John Hodgen and his faculty secured exclusive control of medical service at the St. Louis Hospital, the oldest in the city, operated by the Daughters of Charity. From 1874 onward, the hospital was located on the northernmost fringes of St. Louis at Grand Boulevard and Montgomery Street. Perhaps by way of compensation for the miles of distance between lecture halls and wards, the college cultivated a reputation for excellence in the basic sciences that was to remain its hallmark until the merger of 1899.

Competition between the two colleges in the second half of the century was intensified by the founding of many other medical schools in the region. Between 1855 and 1892, no fewer than
The St. Louis Medical College was housed in a graceful, neoclassical structure at 7th and Clark from 1849 until 1892.

13 institutions for the training of physicians were established in St. Louis alone. The majority of these taught what regular doctors scorned as "sectarian" treatment (e.g., homeopathy and eclecticism) and were relatively short lived. A few, notably the St. Louis College of Physicians and Surgeons, were major competitors and graduated more physicians in some years than the two schools of the Washington University tradition. None save the two institutions that were to merge in 1902 and later join St. Louis University (Beeumont Hospital Medical College and Marion Sims College of Medicine) survived long into the 20th century.

This battle for survival explains why "our" colleges again sought university ties. Missouri Medical College was the first to move in this direction by returning to an affiliation with the University of Missouri in 1886. A "contract of cooperation" between the state Board of Curators and the private college designated the latter to be "section no. 2" of the University Medical School. This meant that entering students were encouraged to matriculate in Columbia, study for one year, then transfer to St. Louis for the remainder of their medical studies. In theory, the contract was designed to assure a steady supply of students for Missouri Medical College while relieving the state of the costs of building and supporting clinical training facilities in Columbia. In practice, however, the expectations of neither institution were satisfied, and the contract was terminated after only four years.

The agreement between St. Louis Medical College and Washington University was announced April 20, 1891. It occasioned little debate or fanfare and dictated few changes. Internal autonomy was preserved; the college was required as before to operate strictly on income from tuition and gifts. Even the name of the college remained the same; "Washington University Medical Department" was added as a kind of subtitle. Greater attention in those days was being given to the construction of a new building, using money raised by the Medical Fund Society. That structure, a wonder of its time with nine laboratories, three lecture halls, and quarters for the O'Fallon Clinic all under one roof, opened at 1806 Locust Street in October 1892.

Meanwhile, Missouri Medical College strengthened its position by absorbing a small specialty college, the St. Louis Post-Graduate School of Medicine and Polyclinic, in 1890. A new building was constructed alongside the Polyclinic, located at Jefferson and Lucas Avenues, that would house the combined institution. Much later, a prominent alumnus, Washington University anatomy professor Robert J. Terry, would recall fondly "the flourishing condition of the college in its new quarters: good laboratories, new equipment, a large clinic and enthusiastic faculty."

The merger of the two oldest St. Louis medical colleges was not inevitable. Many suitors in town sought university backing and generous endowments. Perhaps it was the acquaintance brought about by old rivalry, as well as old money, that brought Missouri Medical College together with St. Louis Medical College in the fold of Washington University. As with the affiliation of 1891, the merger of 1899 was carried out with a minimum of fanfare and disruption of long-accustomed practice.

It was the 20th century that brought massive changes, but that, of course, is another story. When Washington University School of Medicine celebrates the centennial of an event in 1891, it is done with the precision of historical hindsight. Clearly, without university affiliation, St. Louis Medical College and Missouri Medical College would not have continued operating to this day. 

A stylized rendition of a room that seems more than 100 years away from the laboratories of today.
Of the 116 students who graduated from the School of Medicine earlier this year, 106 — fully 92 percent — will be doing their postgraduate training at one of their top three choices of institutions. Those results, from the National Residency Matching Program, reflect a healthy increase over last year, when 83 percent got one of their first three choices. In 1991, 70 percent (81 graduates) matched with their first choice; last year that number was 63 percent.

Again this year, internal medicine residencies were the most popular; 38 graduates will be pursuing that specialty. Pediatrics (17) and general surgery (10) were also leading choices. Six participants selected psychiatry; five chose obstetrics and gynecology; three will pursue family practice.

Forty-five of the new physicians are staying in St. Louis for their post-graduate training, the great majority of them at Washington University Medical Center hospitals. Other popular destinations were California, Pennsylvania and Massachusetts.

The complete list follows. Some names are listed more than once because of preliminary and transitional residencies.

**ALABAMA**

Birmingham  
University of Alabama Hospital  
Deimthuy D. Bui, Internal Medicine Primary

**CALIFORNIA**

Los Angeles  
UCLA Neuropsychiatric Institute  
Mark A. Hassen, Psychiatry  
Charles L. Raison, Psychiatry  
Orange  
University of California, Irvine Medical Center  
Tadd T. Hsie, Family Practice

San Diego  
University of California San Diego Medical Center  
Normal W. Gross, Internal Medicine  
U.S. Naval Hospital  
Douglas R. Trocinski, Surgery  
Stanford  
Stanford Affiliated Hospitals  
Paul C. Hwang, Pediatrics

**CONNECTICUT**

New Haven  
Yale-New Haven Hospital  
Rita A Suri, Psychiatry

**DC**

Washington  
Georgetown University Hospital  
Maral A. Kibarian, Transitional  
Kenneth H. Wong, Obstetrics & Gynecology  
Walter Reed Army Medical Center  
Daniel J. Donovan, General Surgery

**FLORIDA**

Gainesville  
University of Florida  
Cynthia M. Smith, Ophthalmology

**HAWAII**

Honolulu  
Tripler Army Medical Center  
Scott J. McAtee, Transitional

Steve Meeks looks for the envelope bearing his name.
Darrell Fader, David Thorsett and Henry Yang, pleased with Match Day results.

ILLINOIS
Belleville
Scott AFB
Elizabeth A. Martucci, Family Practice
Chicago
Cook County Hospital
Steve L. Meeks, Transitional and Emergency Medicine
Louis A. Weiss Memorial Hospital
Jonathan A. Wyatt, Transitional
Rush-Presbyterian-St. Luke's Medical Center
Edward S. Levy, Obstetrics & Gynecology
University of Chicago Hospitals
Charles A. Lerner, Diagnostic Radiology
INDIANA
Indianapolis
Indiana University Medical Center
John D. Marshall, Anesthesiology
Kimberly D. Pendleton, Pediatrics
IOWA
Iowa City
University of Iowa Hospitals & Clinics
Jonathan H. Hughes, Pathology
Henry P. Yang, General Surgery
KANSAS
Kansas City
University of Kansas
Robert A. Lowenthal, Ophthalmology
MARYLAND
Baltimore
Johns Hopkins Hospital
Joseph A. DiGiuseppe, Pathology
Adam T. Lottick, Internal Medicine
Raquel M. Pionkowski, Emergency Medicine
Sinai Hospital
Jonathan D. Boniuk, Internal Medicine Preliminary
University of Maryland
Tonya D. Tuggle, Psychiatry
MASSACHUSETTS
Boston
Beth Israel Hospital
Marcella Kuhlman, Internal Medicine
Boston City Hospital
William M. Weston, Emergency Medicine
Angela De Michele shares her happiness with a friend on Match Day.
Edgar L. Engels, Jr., M.D. '81, and Edgar L. Engels, Sr., M.D. '36, father and son.
Alumni Achievement Awards

Ronald G. Evens, M.D.

Ronald G. Evens is Elizabeth E. Mallinckrodt Professor and head, department of radiology, and director of the Mallinckrodt Institute of Radiology. He is also adjunct professor of medical economics at Washington University and radiologist-in-chief at Barnes and Children's Hospitals.

At age 31, Evens was the youngest person ever to be named department head at the School of Medicine. Under his able leadership, the Mallinckrodt Institute has experienced major expansion.

Concurrently with his duties in the department of radiology, Evens served as president and chief executive officer of Children's Hospital from 1985-1988 and as vice chancellor for financial affairs at Washington University from 1988 to 1990.

Evens has published extensively in professional journals and textbooks, and is a member of editorial boards for a number of publications, including the Journal of the American Medical Association.

To all his responsibilities, Evens has brought extraordinary skill and energy, especially to the Washington University Medical Center Alumni Association, for which he served as president during 1988-1989.

Lawrence W. O'Neal, M.D.

Lawrence W. O'Neal is director of quality management for the Sisters of Mercy Health System in St. Louis, with responsibility for the development and maintenance of a quality management program in 14 acute care hospitals in seven South Central states. Throughout his career he has devoted himself to excellence in health care as surgeon, researcher, administrator, and teacher, and he has contributed enormously to the fields of endocrinology and endocrinological surgery.

O'Neal has combined a busy private practice with his academic activities. From 1954 until 1966 he was assistant in clinical surgery at Barnes Hospital. In 1969 he was appointed assistant professor in clinical surgery at the Washington University School of Medicine. He became an associate professor in 1971.

O'Neal is the author of the book, Surgery of the Adrenal Gland, and co-editor of The Diabetic Foot, now in its fourth edition.

O'Neal has been active in many community health activities and in civic organizations. He has been a member of the advisory committee of the St. Louis Area Chapter of the March of Dimes and the Mayor's Search Committee for Health Commissioner.

Meredith J. Payne, M.D.

Meredith J. Payne is clinical assistant professor of plastic surgery at the St. Louis University School of Medicine and teaches at John Cochran Veterans Administration Hospital, where she is chief of the department of plastic surgery. She combines this responsibility with a busy private practice in which she has engaged since 1957.

She holds the distinction of being the first woman to be board certified in both general and plastic surgery. She is currently serving her second term as president of the St. Louis Area Society of Plastic Surgeons and is active in the Missouri State Medical Association, serving as vice-councillor. Payne has also given many years of service as a member of the executive council of the Washington University Medical Center Alumni Association.

Payne was one of the first women to enter surgery, and
she has been a gentle, but persuasive, groundbreaker for women who came into the field after her. Peers, students and friends invariably describe Payne as “gracious, involved, concerned, always willing to help.” Those sentiments are echoed by her patients, who view her with great gratitude and affection.

**Alumni/Faculty Awards**

**Nicholas T. Kouchoukos, M.D.**

Nicholas T. Kouchoukos is John M. Shoenberg Professor of Cardiovascular Surgery at the Washington University School of Medicine, surgeon-in-chief and cardiovascular and thoracic surgeon-in-chief at The Jewish Hospital at Washington University School of Medicine.

Kouchoukos has four times received the Physician’s Recognition Award from the American Medical Association and in 1981 was named Physician of the Year by the Hellenic Medical Society of New York. He is a member of several honorary societies, including Phi Beta Kappa and Alpha Omega Alpha.

In 1985-86, he brought his dedication and skill to the presidency of the Washington University Medical Center Alumni Association.

For all his achievements, Kouchoukos is known as a gentle, quiet man. The words of his peers and students testify to their esteem: “He is the most dedicated, hard-working person I have ever known.” “He is a true gentleman, wonderful to work with.” “He listens to everyone’s point of view, and somehow he brings harmony to the most difficult situations.”

**H. Mitchell Perry, Jr., M.D.**

H. Mitchell Perry, Jr. is professor of medicine and director of the hypertension division, department of internal medicine, Washington University School of Medicine. From 1963-1976 he was chief of the medical service at the John Cochran Veterans Administration Hospital. Since 1976, he has been national physician-coordinator for hypertension for the Department of Veterans Affairs, Washington, D.C.

Internationally known for his groundbreaking research on the causes and treatment of hypertension, Perry has been especially interested in helping patients, particularly impoverished and minority ones, take responsibility for controlling their own blood pressure.

Perry is esteemed not only as researcher and clinician but as distinguished, dynamic teacher and concerned community citizen. His many honors include the Louis B. Russell Award for service to minority and low-income communities and, this year, the Edward Freis Award from the National Conference on Cholesterol and High Blood Pressure Control.

**Jessie L. Ternberg, Ph.D., M.D.**

Jessie L. Ternberg is professor of surgery at Washington University School of Medicine. From 1972-1990 she was pediatric surgeon-in-chief and director of the division of pediatric surgery at St. Louis Children’s Hospital.

Ternberg performs more than 600 surgeries each year, and is nationally known for her expertise in the area of correcting congenital gastrointestinal deficiencies in children. She is one of the few pediatric surgeons in the country to successfully separate Siamese twins. No one speaks of her with more appreciation and affection than her patients and their families. Her students call her “an inspiration,” and stay in touch with her long after graduation.

Her first research was published in 1949. Since then, she has written or co-authored scores of papers, abstracts, book chapters, and a book, A Handbook for Pediatric Surgery.

Throughout her career, Ternberg has met prejudice against women in medicine with dignity and determination, quietly using her masterful surgical skill and dedication to her patients’ welfare to convert skeptics into her admiring supporters.

**Distinguished Service Award**

**William J. Harrington, M.D.**

William J. Harrington is Distinguished University Professor at the University of Miami School of Medicine. He chaired the department of medicine there from 1964-1978, developing a fledgling department into one of national repute. He later directed the division of hematology for six years.

In 1950, Harrington came to Washington University School of Medicine as a National Cancer Institute Trainee under the late Carl V. Moore, M.D. Here he conducted his now infamous experiment, testing his theory that autoimmune factors played a major role in idiopathic thrombocytopenic purpura. A young woman suffering from the disorder was admitted as a weekend emergency; her blood and Harrington’s were compatible. Confronted with this opportunity, he received a unit of her blood and gave his to her. His platelets did not survive in her blood; hers caused a rapid and profound deterioration of his.

This was the first clear-cut demonstration of a humoral autoimmune factor.

Moore, having learned of this dramatic event, promptly admitted Harrington to the hospital, where, happily, he recovered.

Harrington has combined significant research activity with his academic responsibilities, fulfilling the promise of his early years when, at age 28, he became the youngest researcher ever elected to the elite American Society for Clinical Investigation.
Del Harris, M.D. '51, and Dorothy D. Reister, M.D. '50, in the spirit.

The alumni association gavel passes from Joseph F. Ruwitch, Jr., M.D. '66, to Ira J. Kodner, M.D. '67.


A scientific program session.

Frances Zimmerman, Herbert Zimmerman, M.D. '51, Kenneth D. Serkes, M.D. '51, and Margaret Bischof Serkes, M.D., renew acquaintances.
Incoming alumni association president Ira J Kodner, M.D. '67, converses with Washington University Chancellor William H. Danforth, M.D., and Virgil Loeb, Jr., M.D. '44.

Julius M. Shier, M.D. '41, makes a point to Samuel E. Schechter, M.D. '41.

Robert C. Buckner, M.D. '41,
Philip W. Bernstorf, M.D. '41,
Betty J. Bernstorf and Harry B. Stauffer, M. D. '31.
June King, Alan Koch, Muriel Koch and M. Kenton King, M.D.

William J. Harrington, M.D., receives the Distinguished Service Award from Dean William A. Peck, M.D.

Mitchell Yanow, M.D. '41.

Betty Perry, H. Mitchell Perry, Jr., M.D. '46, (recipient of the Alumni/Faculty Award) and Nicholas H. Nauert, Jr., M.D. '46, examine the reunion program.

David Buerger, M.D. '91, this year's class president.
Dean William A. Peck, M.D., presents the Alumni Achievement Award to Ronald G. Evens, M.D. '64.

Isabel G. Parish and Havner H. Parish, Jr., M.D. '56, visit with a friend.

Members of the Class of '81 and their guests.
Ruth C. Dickinson, assistant vice chancellor for medical alumni and development programs, chats with Melvin R. Kaplan, M.D., and Harriet Smith Kaplan, M.D. '56.

Janis Carter, Marianne O'Neal and Lawrence W. O'Neal, M.D. '46.

Meredith J. Payne, M.D. '50, receives the Alumni Achievement Award from Dean William A. Peck, M.D.

Samuel B. Goree, M.D. '45, Ronald G. Evens, M.D. '64, and Hanna Evens greet one another.
James C. Sisk, M.D. '46, and Albert Rauber, M.D. '46.

William J. Harrington, M.D., Virgil Loeb, Jr., M.D. '44, and James C. Sisk, M.D. '46.

Oenophile Boyd Hayward, M.D. '46.

Mary Moreland and Joseph I. Moreland, M.D. '41, share a dance.

Ann Galakatos (left) and Deborah Ott shared a lighter moment at commencement exercises, held Friday, May 17, on the Hilltop Campus. The School of Medicine granted 10 M.D./Ph.D. degrees, seven M.D./M.A. degrees and 99 M.D. degrees.
Single-lung transplant surgery, as developed in Washington University School of Medicine’s lung transplantation program, is successfully restoring vitality to pulmonary hypertension patients. The procedure represents the most encouraging advance in treating the debilitating disease in almost a decade.