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Making Bones
The School of Medicine has published an independent annual report for 1991. Taking the theme "Then and Now," the report treats the first 100 years of the medical school on the occasion of the centennial celebration. Copies of the report are available from Medical Public Affairs, Box 8065, 660 South Euclid, St. Louis, MO 63110, or by calling (314) 362-8258.
Like The Salamander’s Tail

A reconstructive plastic surgeon and molecular cell biologists collaborate to perform an alchemist’s feat.

Leadbelly And Friends

A medical school anatomist and anthropologist comes back from Namibia with the find of a lifetime.

Sending The Wrong Message

When parts of chromosomes swap places, the results can be malignant.

Celebrating Excellence

A photographic retrospective of the centennial celebration captures the breadth and depth of the festivities.

Newsbriefs

Personal Outlook

Silhouette

Alumni Report

On The Cover:

Putting the techniques of molecular cell biology into action, microsurgeon Roger Khouri, M.D., transforms one of the body’s rich resources — muscle — into one of its more precious components — bone. Artist Greg Michaels illustrated the process for Outlook.
Donors Present Library With 18th Century Herbal

The archives and rare books division of the Washington University Medical Library has received the gift of a set of four 18th century volumes on medicinal plants, called an herbal. The vellum-bound volumes, containing 1,250 brilliantly hand-painted plates of fruits, flowers, trees, shrubs and herbs, were published in Regensburg, Germany, from 1737 to 1745. In its near-perfect condition, the work is valued at approximately $100,000.

Titled *Phytanthozayina Iconographia sive conspicus...*, the herbal was the gift of Jean Frederick Rogier, M.D., and his wife Verna Dorothea Rogier. Rogier is a graduate of the medical school's class of 1934. "This is a superb addition to the collection and a magnificent gift for which we are deeply in the Rogiers' debt," says Susan Alon, rare book librarian. "It's a coup for the collection."

Compiled by Johann Wilhelm Weinmann, an apothecary, the herbal was executed at a time when the production of such large folio compendiums, particularly in anatomy and botany, was at its zenith. The book's manufacture represents a dozen years of labor by many skilled artists.

The books originally served as essential references for physicians of the day, who relied almost exclusively on botanical preparations as medicines. Remarkably, the volumes presented to the school by the Rogiers are in flawless condition, their colors still bright and their binding papers unblemished. In addition to the color plates, the books include an index, a description of each plant and its various types, a history of its uses and directions for its pharmacological preparation.

The books came into the Rogier family from Jean Rogier's mother, Stella Suppiger, whose forebears emigrated from Switzerland to the United States in 1831, eventually founding the town of Highland, IL. It is likely that the travelers carried the 10-by-15-inch volumes with them on their journey by schooner from Le Havre to New York, up the Hudson River, through the newly opened Erie Canal and down the rivers to St. Louis.

Dressed To Kill In Designer Genes

New plant genetic engineering techniques are creating hardy crops that may soon take on the traits of the Terminator, rendering the benevolent image of the Jolly Green Giant obsolete. Gardens of the future may be full of plants that have been genetically programmed to fight off and even kill predatory insects. This new breed of plant may be more effective, and safer, than the countless thousands of tons of insecticides and pesticides farmers now use, says plant genetic engineer Wayne M. Barnes, Ph.D. "In the long run, perhaps the best way to defend our crops is to put genes for insecticides into plants, making them able to defend themselves from insects," says Barnes, associate professor of biochemistry and molecular biophysics. "Right now we're pouring incredible amounts of chemicals onto plants and into the land. It's overkill."

Recognizing the dangers of pouring chemical pesticides onto the land, researchers like Wayne M. Barnes, Ph.D., genetically engineer plants that can defend themselves against predatory insects. Barnes uses tobacco plants as models for what can be done with more vital crops.
Already, tobacco plants raised in Barnes' lab use their own brand of naturally produced insecticide to fend off voracious caterpillars. Some of the plants are even clever enough to produce the toxin only in self-defense, after they've been wounded by an insect.

The tobacco plants are armed with the gene for Bacillus thuringiensis (Bt), a natural bacterial insecticide that can be purchased in most garden shops. The Bt protein is completely safe to humans, but deadly to caterpillars of the order Lepidoptera, which includes moths and butterflies.

"When a caterpillar eats a leaf, this leaf that it has evolved to love is suddenly poisonous, and the insect dies," Barnes says. The toxin takes a day or two to work, but that drawback is compensated for by the fact that the insecticide is completely safe to humans. "People can dust Bt on vegetables or eat it in yogurt as a protein supplement. It's that safe," he says.

As a plant genetic engineer, Barnes' job is to improve what nature has to offer. But he admits that Mother Nature is a first-rate plant genetic engineer and has provided him with some of his most useful genetic tools.

One such tool is Agrobacterium tumefaciens, a bacterium named for its ability to shuttle cancer genes into tobacco plants. Barnes exploits this natural ability. "We've deleted the bacterium's tumor-forming genes and put in our Bt genes," he explains.

In order to tell that the Bt gene is in the plant, Barnes turns to nature again, this time to borrow the glow of the firefly. He splices luciferase — the gene that makes fireflies glow — into the A. tumefaciens DNA containing the Bt gene. The tobacco leaves that take up the insecticide cast an eerie greenish glow when dipped in luciferin, the other chemical needed to give fireflies their spark. "That glowing shows that the Bt gene is in the leaves," Barnes notes. "With natural tobacco, nothing happens."

Sometimes, though, the plants don't glow unless the leaf is wounded first. This could well show that production of the insecticide is wound-inducible, meaning it is not produced until the plant is gnawed by insects, Barnes says. "This is good, because it means the gene would normally be off. The gene is only turned on after the insect begins chewing on the leaf," he explains.

Although the gene works well in tobacco plants, improving tobacco crops doesn't appeal to Barnes. "Tobacco is only a test, kind of a lab rat," he says. Instead, he would rather improve broccoli, corn or tomatoes, crops that are staples around the world. He already has sent the gene to Cornell University colleagues, who are trying to put it into broccoli. Others are working on putting it in walnuts and large trees, he adds.

Crane, Clayton And Smith Assume New Roles

James P. Crane, M.D., has been named an associate vice chancellor and associate dean for clinical affairs; Donald E. Clayton has been named an associate vice chancellor, and Morton E. Smith, M.D., has been named associate dean for postgraduate education.

The appointment of Crane, effective October 15, was announced by William A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine. "There is no one better qualified than Doctor Crane, both professionally and personally, to undertake this crucial new activity. He is a highly accomplished clinician, teacher, investigator and administrator, and we are most pleased that interactions with hospitals, managed care systems, corporations, government agencies and the lay community. He will also assist in the development of a new ambulatory care center to be located adjacent to Barnes Hospital and the School of Medicine. The programs he develops will be geared toward improving health care in the region.

According to M. Frederic Volkman, the university's vice chancellor for public affairs, Clayton now will serve as associate vice chancellor in addition to his ongoing duties as executive director of medical public affairs. He oversees all aspects of the School of Medicine's public affairs operation, supervising a staff responsible for medical news and feature writing, publications, photographic services and local and national media relations.

"Don Clayton has been an invaluable asset to the Washington University public
**Starving The Malaria Bug**

A new class of medications designed to starve an army of hemoglobin-chewing parasites could provide a much-needed alternative drug therapy to combat malaria, a fever-causing illness that kills 2 million people annually.

The anti-malarial drugs, if successful, would block the feeding of the parasites that cause the disease, says Daniel E. Goldberg, M.D., Ph.D. Goldberg devised the new approach and is designing compounds that essentially deceive the parasites into "believing" they are destroying hemoglobin, the oxygen-carrying component of red blood cells.

Once they enter the bloodstream, malaria-spreading organisms burrow into red blood cells, incorporating themselves in the cells' hemoglobin-rich cytoplasm. There, the parasites devour hemoglobin, turning the molecule's building blocks into fuel for further forays.

The parasites that cause malaria are notorious for their voracious appetite. "In just a few hours they will chew up a quarter pound of hemoglobin in a heavily infected patient," says Goldberg, an assistant professor of medicine. Fortunately for them, they are in a rich environment: It's a little bit like a child locked in a candy store."

For the most part, Americans are sheltered from the human die, most of them children.

A puzzling feature of this disease is that people who carry sickle cell anemia or thalassemia genes — those whose hemoglobin is misshapen — are protected from malaria. Most people aren't protected, however, and so must rely on the drugs chloroquine or mefloquine. In the last few years, though, protection has become much more difficult.

"It used to be a straightforward affair," Goldberg says. "You would take your chloroquine pill once a week starting just before going out of the country, weekly once you were there, finishing up once you got back. Now, though, the parasites have developed resistance to the drug. Chloroquine resistance is rampant in most endemic areas and becoming worse." With chloroquine obsolete in most of the world, the search is on for better medications. In the meantime, Goldberg notes, most people are relying on mefloquine.

But mefloquine isn't meeting with much success either. "Mefloquine resistance has already cropped up and can be expected to spread in short order," he says. "There's a desperate need for new chemotherapeutic agents."

Goldberg's work may relieve dependence on mefloquine-type medications by making it possible to fashion drugs that could starve malaria-causing parasites. "If the organism can't chew up hemoglobin and can't grow, it will die rapidly," Goldberg says.
Sick Infants May Need Even More TLC

To a small, sick infant, the routine act of changing a diaper may evoke as painful a response as a needle piercing its spine, says a researcher who studies pain in newborns.

Taking a temperature, checking blood pressure or placing an X-ray plate under the body — medical procedures typically considered innocuous — may cause physiological responses in premature and/or sick infants similar to those elicited by adults in pain, says Fran L. Porter, Ph.D., assistant professor of pediatrics. Because this group of newborns is so developmentally different from older children and adults, Porter says experts may need to rethink their definition of pain for this special group.

Porter studied 77 infants, all of whom required neonatal intensive care and were monitored for their physiological responses to receiving a lumbar puncture. Half received anesthesia, half did not. A lumbar puncture, which adults consider painful, is routinely performed with anesthesia in adults and older children. Infants routinely are given anesthesia during surgical procedures. For bedside procedures like the lumbar puncture, anesthesia has not been commonly used because of long-held beliefs that infants do not feel pain.

"We looked at a variety of measures to determine the infants' responses to the procedure, because in infants there is no single method to identify pain," Porter notes. "In older populations, pain is assessed primarily by self-report. We tell our physician that we have pain, how it feels, its intensity and duration. Babies cannot do that."

This study reports physiological changes in heart rate and respiratory rate, both of which are known to show change in response to pain in older populations. The researchers also monitored oxygen and carbon dioxide levels in the blood, which can be affected by stress.

Prior to the procedure, the infants were monitored undisturbed in their nursery beds for 10 minutes. During the preparation phase, the babies were turned onto their sides in a fetal position so their backs could be sterilized at the site of the lumbar puncture. The infants were then flexed and held firmly so the needle could be safely inserted into the back. They remained in the flexed position during the actual lumbar puncture.

"There were no differences between the control group and the anesthetized babies on any physiological measures while receiving the lumbar puncture," Porter notes. "We expected the anesthetized babies would show greater physiological stability during a lumbar puncture than those without the anesthesia. What we found with all of the babies in the study was that the change from baseline to the preparation period was very dramatic, with significant increases in heart rates and decreases in breathing rates. But during the lumbar puncture, which we considered to be the painful procedure, their heart rates actually slowed down from where they had been."

When the babies were flexed, their heart rate increased an average of 13 beats per minute. In addition, their respiration and oxygen levels decreased significantly. During the lumbar puncture, their heart rates dropped eight beats per minute, returning toward baseline and there was no further change in respiration. "If anything, it looked like they were calming down," she says.

Porter believes stress, resulting from the flexed position the infants were in for the procedure, may explain the dramatic responses during preparation.

"Flexing the baby exposes the spine so the spaces between vertebrae are as wide as they can be," she says. "The baby is maintained in this position throughout the preparation period and the lumbar puncture. This necessary flexed position may cause changes in the baby's airway, or, if..."
On The Move

Researchers have known for years that when skin is injured, the immune system's T cells set out on a difficult mission — to break out of blood vessels, climb through the skin's layers and get to the injury where they fight infection and promote healing. What scientists haven't known is exactly how T cells make the trek. A recent study provides convincing evidence that T cells use molecules on their surfaces, called integrins, like tiny hands climbing a ladder to move through dense skin tissue.

During a T cell's journey, "it's not floating through an inert gel. It's maneuvering its way through a jungle of connective tissue," says Thomas Kupper, M.D., associate professor of medicine in dermatology. Researchers have known that T cells somehow bind to skin's structural proteins and that the integrins on their surfaces interact with those proteins. Some researchers believed that T cells must use integrins to move through tissue, but until now no one had found a convincing way to test the theory.

Kupper and Thomas Ferguson, Ph.D., assistant professor of ophthalmology and pathology, used mouse T cells programmed to respond to a particular chemical. When those T cells were injected into mice that had been exposed to the chemical applied to their ears, the cells migrated to the ear and produced an irritation — the normal and expected immune response. But when the T cells were first mixed with peptides that blocked their integrins, they did not produce an irritation.

"If you add those peptides... the T cells behave very differently and don't migrate out of vessels into skin to generate an inflammatory response. That, to our minds, validates the idea that T cells must use these integrins to climb over the matrix proteins to get where they are going," Kupper explains.

The treated T cells could still react to the chemical in a test done outside of the mice, suggesting that in live mice the cells were ineffective because they never made it to the ear, not because they couldn't respond to the chemical at all.

Kupper emphasizes that the study does not explain exactly where T cells are stopped along their migration route. "That we are still dissecting out, and it's a fairly difficult determination to make. But we know that we've turned off the end result," he says.

The study eventually may point the way to therapies for many diseases in which T cell migration plays a part, such as rheumatoid arthritis and inflammatory bowel disease. These diseases develop when T cells migrate — as they do in skin — out of blood vessels and into body tissues, where they cause damaging inflammation.

AIDS experts from across the country joined local healthcare workers in St. Louis early in October to discuss recent advances in AIDS management and HIV surveillance findings. People living with HIV discussed their personal feelings, and members of the activist group ACT-UP were on hand. The Centers for Disease Control estimates that 1 million people in the U.S. are now infected with the virus. Here, Sue Wightman, R.N., B.S.N., coordinator of the outreach program for the AIDS Clinical Trials Unit at Washington University, poses with a portion of the Names Project AIDS Memorial Quilt that was on display as part of the clinical symposium.
Where Are They Now?

Barbara J. Fox, co-author of a recently published paper that reports the career development of graduates of Washington University's Medical Scientist Training Program (MSTP), says the project was born out of a desire to keep track of the lives of the students to whom she had become attached. "I knew everything about the students, handled everything they needed and cared about them. Then, when they graduated, suddenly I didn't know what was going on in their lives," says Fox, assistant director of the MSTP.

In the early days of the program, she spoke regularly with graduates by phone, but as their numbers increased that became impossible. Slowly, her information gathering became more formalized: today a standardized questionnaire goes out each year to every graduate. The codified results from the questionnaires, 90 percent of which are returned, make up the data for the paper, "Career Choices of Graduates from Washington University's Medical Scientist Training Program," published recently in the journal Academic Medicine.

Results are both impressive and surprising. Since the first graduates left the program here in 1974, more than 95 percent of the total have pursued residencies rather than postdoctoral work. The vast majority chose clinical residencies, with 44 percent training in departments of medicine. Leaving pure science for clinical residencies has neither diluted the graduates' interest in research nor slowed their careers, however.

Of the 72 graduates who had completed their training by 1990, 62 were employed by academic institutions and two were NIH investigators. Remarkably, 16 were associate professors, three were assistant professors and two were instructors. Fox reports. Of the 62 in academic careers, 43 had NIH support for their work. The paper says: "The demand for such students appears to be great, and they experience little difficulty in finding appropriate positions."

Washington University's MSTP is the nation's largest, training medical scientists in a six-year program that awards both M.D. and Ph.D. degrees. Fox's co-author, Carl Frieden, Ph.D., stepped down as director of the program on October 1, handing the reins to Stuart A. Kornfeld, M.D., the fourth director in the program's 22 years.

High Honor To Atkinson

John P. Atkinson, M.D., professor and head of the division of rheumatology has been awarded the 1991 Alpha Omega Alpha Distinguished Teacher Award. Alpha Omega Alpha (AOA), a professional medical honor society, gives the national award each year to recognize outstanding accomplishments in teaching clinical sciences to medical students.

Atkinson, the fourth to ever receive the honor, is especially pleased because recipients are nominated by their colleagues. "This indicates that fellow faculty members and students appreciate one's teaching efforts. Teaching students is an activity that I enjoy; I am lucky that the subjects I teach are the same ones that I study in the laboratory and the clinic," he says. Atkinson teaches immunology and the diagnosis of rheumatic diseases to first- and second-year medical students and conducts teaching clinics with third- and fourth-year students.

Each medical school in the country may nominate one faculty member for the award. Atkinson was chosen by William A. Peck, M.D., vice chancellor and dean of the School of Medicine, with input from faculty and students. In his nomination letter Peck writes. "He is an unusual lecturer who is capable of combining humor, enthusiasm and energy in his teaching style in a manner that makes students want to learn." Students, the letter states, praise Atkinson for being courteous, compassionate and putting his students at ease.

Atkinson has been recognized for outstanding teaching before. In 1980, the Washington University Department of Medicine named him teacher of the year, and in 1986 he was named teacher of the year by the medical school senior class.

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John P. Atkinson, M.D., has been honored for his accomplishments in teaching clinical science to medical students.

Members of AOA and the Association of American Medical Colleges (AAMC) chose the recipient. Atkinson received the $2,500 award November 10 at the AAMC annual meeting in Washington, D.C.
The alchemists of the Middle Ages aimed to transform base metals into gold and sought a universal cure for disease. Although their results fall short of those unrealistic goals, medical scientists now can transform one type of tissue into another more valuable form. By combining their techniques, plastic surgeons and cell biologists are performing the wizardry of changing a commonplace flap of animal muscle into a bone in exactly the shape they need. Soon, they may have the body using its natural processes to create the replacement parts it requires.

According to Roger K. Khouri, M.D., assistant professor of surgery, among human tissue, bone in particular has been difficult for medical science to master. For almost 60 years, scientists have worked to stimulate bone formation within muscle via the introduction of any one of a number of substances, from alcohol to a synthetic sponge.

But the knowledge that bone formation could be induced remained experimental and without an essential usefulness because where bone was badly damaged, the muscle surrounding it also often was deficient and not suitable as a substrate.

The shape and location of the bone that sometimes could be made to form also remained unpredictable. "A pellet of bone in a muscle is almost always a bad thing," as Khouri says.

Meanwhile, reconstructive plastic surgeons have struggled to treat skeletal defects — both traumatic and degenerative — because there is so little bone to spare for the purpose of transplantation. "Bone has a limited ability to regenerate. Where the surrounding tissue has been damaged by heavy trauma or radiation, or the bone deficit is large, we've had only the fibula (the non load-bearing bone of the lower leg) and the iliac crest (the hip bone) available to transplant as a replacement live bone," Khouri says. "And those are big operations entailing considerable pain that can only be performed by highly trained surgeons."

Because of the complexity and morbidity of the surgery required and because of the material's inherent inflexibility to be shaped precisely, bone transplantation has lagged behind muscle and skin grafting in medicine's arsenal of restorative techniques.

Reconstructive plastic surgery rests on the principle of "borrowing from Peter to
Microsurgeon Roger Khouri, M.D., and his colleagues have combined their skills to develop a technique whereby cells in muscle tissue are transformed into bone. Using the technique, researchers soon may coax the body into producing its own replacement parts.
The Technique

In the classical understanding, Khouri explains, both bone and muscle derive from cells of the same layer of the embryo: the middle, or mesenchymal, layer. (The skin and nerves spring from cells of the outer [ectodermal] layer, and the internal organs are built from cells of the inner [endodermal] layer.) Under genetic control, groups of cells from each layer form the specific structures and tissues of the body as development proceeds.

Cell determination, the process by which a cell with several potential fates is instructed to assume one specific fate, has been difficult to study. But scientists have long seen evidence to support the belief that around adult muscle cells reside other cells not yet differentiated into a precise type and still capable of more than one fate, though they are different from the earliest mesenchymal cells. These cells are called “pluripotent” for their ability to develop into one of several types. Throughout a life and in motion, a cell with several potential fates is instructed to assume one specific fate, has been difficult to study. But scientists have long seen evidence to support the belief that around adult muscle cells reside other cells not yet differentiated into a precise type and still capable of more than one fate, though they are different from the earliest mesenchymal cells. These cells are called “pluripotent” for their ability to develop into one of several types. Throughout a life and in response to certain stimuli, the body occasionally directs some pluripotential cells to differentiate, Khouri says.

The exact nature of the cells that can be induced to become bone remains speculative, but during the last few years, cell biologists have identified seven glycoproteins normally present in bone that stimulate the cells. Called bone morphogenetic proteins or BMPs, each of the seven can act as a chemical trigger for beginning the process of turning pluripotential cells to bone.

The most powerful and task-dedicated of the seven, BMP-3, was identified by Hari Reddi, Ph.D., of The Johns Hopkins School of Medicine, a collaborator of Khouri’s. Reddi dubbed the glycoprotein he identified “osteogenin,” for its ability to induce bone generation. Reddi and Khouri also refer to osteogenin as a "educated guesswork and trial and error,” he says. Eighteen of the muscle flaps received the osteogenin; five, serving as controls, got only the carrier. The 18 also were coated with demineralized bone matrix (DBM), essentially powdered rat bone with the calcium chemically removed. That technique, according to Reddi’s research, also induces bone forma­tion and provides a synergistic boost to the action of the osteogenin. As osteogenin has become more available, the researchers have stopped using the DBM.

The hinged molds, filled with the muscle tissue, then were closed, with access provided for the vein and the artery that supplied the muscles. Khouri surgically implanted the molds in pockets in the rats’ abdominal walls, “simply as a convenient place to put them.”

Ten days later, the molds were removed and opened to reveal in the 18 a “rigid, gritty, bony” tissue that retained the precise details of the molds. The control flaps were shapeless and showed no ossification. “All of the muscle had changed to bone, complete with marrow,” Khouri says. “The muscle cells either atrophy or just disappear, we are not certain. But the source cells for the bone are clearly cells abundant in muscle tissue. That’s something we could not say with certainty before.”

Reddi and Khouri postulate a “biological cascade” of five steps in the muscle to bone transformation. First, the osteogenin causes pluripotential cells in the muscle to migrate to the site of the protein. Once assembled, the second step is for those cells to multiply by dividing at a rapid pace. Third, they change their structure and realign into cartilage-like tissue, without a blood supply. Fourth, the cartilage turns to bone as blood vessel invasion from the existing supply vascularizes the tissue. And finally, marrow formation occurs within the bone just as it does during early development. “The osteogenin we inject on day one is probably gone by day two, but the cascade of bone development has been set in motion,” Khouri and Reddi say.
A photomicrograph of the tissue that results from the transformation reveals the presence of all of the elements normally found in bone, including marrow (the open areas between the denser meshwork of cancellous bone). (Copyright 1991, American Medical Association. Reprinted with permission, Vol. 266, No. 14, p 1954.)

The Application

The bone that results is cancellous, or sponge-like, in nature and not suitable for weight-bearing applications, Khouri says. But experience with cancellous bone tells him that when it is placed under stress, spongy bone has the capacity to reorganize into cortical, weight-bearing bone. "Under loading pressure and piezoelectric effects, bone cells reorganize along the lines of stress. It's a masterpiece of engineering in which the cells develop a perfect stress-bearing pattern," Khouri says. Experimental evidence suggests that the induced, cancellous bone is capable of the same reorganization.

Khouri anticipates that the evolution of the osteoinduction technique includes two practical steps and a third, more remote, possibility. First, he thinks the technique will challenge and eventually replace autogenous bone grafting, the current gold standard for bone replacement techniques. In a bone graft, small chips taken most often from the iliac crest form a sort of "bridge" across which viable bone cells slowly grow toward one another, spanning the damaged section of bone in a process called creeping substitution.

The fully vascularized bone made via induction of a muscle — preshaped and ready — presents a clear advantage. "This bone comes in with its own blood supply and heals just as a fracture would," Khouri explains. The morbidity and extra surgery involved in harvesting the chips also is spared.

Second, Khouri anticipates that the osteoinduction procedure soon may be used to manufacture needed spare parts in vivo — parts such as mandibles, long bones and even femoral heads, the hip joint bone that so often requires replacement. Because the tissue involved arises from the patient, no threat of rejection looms, and Khouri's only concern is that the transformed bone will be strong enough to bear the load required.

Farther into the future lies the possibility of using the same technique in the treatment of systemic disease. Khouri ponders what would happen if osteoinduction were employed as devised except that mineral deposition was blocked. Then, only marrow formation would occur. Could a patient regenerate his own bone marrow from a flap of muscle, recreating the essential stem cells that produce so many of the elements in blood? "That's something to dream about," he says. The first step is to move the technology from the animal model into human experience, Khouri's next project.

To describe the impact of the leap involved in getting human beings to produce their own replacement parts, Khouri calls upon a favorite creature of the alchemist of a thousand years ago: the salamander. "Cut off the salamander's tail, and he grows it back," he says. "We have lost that ability. But with a better understanding of biology and the judicious use of microsurgical reconstructive techniques, we may be able to regain it. We grew the original, maybe we can grow more."


Leadbelly And Friends

Unearthing What May Be The Missing Link

By Robert Lowes

Glenn C. Conroy, Ph.D., cradles the jawbone that is having a heavy impact on the thinking of paleoanthropologists.
When Glenn C. Conroy, Ph.D., first met him in the Otavi Mountains of southern Africa, Leadbelly was just a grin in an ancient rock. But the yellowed jaw and the blackened molars encased in that rock, Conroy suspected, would have something important to say about man’s ancestors.

Today, Conroy is grinning. The professor of anatomy at the School of Medicine finally has a bone of his own, as they say in paleontology. And it promises to rewrite our notions of human evolution.

Conroy, also a professor of anthropology, headed an expedition that discovered the fossilized jawbone on June 4. He believes that it belonged to a primate that lived in what is now Namibia 13 million years ago, during the Miocene epoch. The animal, nicknamed Leadbelly, may have been a long-sought-after ancestor of both great apes and humans, which together compose the hominoid primates. If this hypothesis proves correct, the jawbone would represent a new Miocene hominoid and the first ever found in subequatorial Africa. Move over, Kenya, as the mother of prehistoric graveyards.

“It’s as if someone went to the Amazon and found a lost tribe of New Zealanders,” says Conroy. “Even though they’re human, they’re not supposed to be there.”

The jawbone has made evolutionary news of another sort—paleontologists are abandoning primitive rivalries to cooperate in the name of science. The field is famous for intrigue and acrimony, partly because “there are more paleoanthropologists than specimens,” says Conroy. (Paleoanthropologists study fossils of all life forms; paleoanthropologists, like Conroy, specialize in human forerunners.) Conroy has insisted that his expedition share the honors for the Namibian fossil. The person who picked it up off the ground was Martin Pickford, a British paleontologist with the College de France.

Only the recent Namibian find places man’s ancestors from the Miocene epoch south of the equator, as this map of Eurasian fossil sites indicates. The fossil represents a major range extension for Miocene hominoids. The site of the recent discovery is known as Berg Aukas, and the graph shows millions of years before the present.

Conroy targeted the arid, sparsely populated country based on educated hunches. Its cave-riddled limestone formations resemble others in South Africa where australopithecine bones have been unearthed. Tantalizing clues of primate fossils have cropped up in mining and geologic reports. Reconnaissance missions by Conroy yielded more provocative evidence. Then there was the desire to break new ground—understandable because more established paleontologists tend to keep the old ground to themselves.

“Where in Africa can I go, where no one else has gone?” Conroy recalls asking himself. He finally convinced the National Geographic Society to underwrite an expedition to Namibia consisting of himself and John Van Couvering, a geologist from the American Museum of Natural History in New York. When Pickford and paleoanthropologist Brigitte Senut, his colleague at the College de France, asked to come along, Conroy said yes.

The group of four convened in Namibia’s capital city of Windhoek on June 4, 1991, and drove six hours to a lead-mining compound in the Otavi Mountains. The mine was closed, but the mining company maintained a station on the grounds. Conroy’s group had permission to stay there while exploring the surrounding mountains. But one destination was just yards away. Near the abandoned mine on a steep slope lay several acres of mine dumpings. The rubble was dotted with chunks of breccia, a pinkish “concrete” of rock and sand that had collected in the area’s limestone caves. Breccia is a rich sediment for fossils, since prehistoric animals often fell into limestone caves or were dragged inside by predators.

Late on the afternoon of their first day, the expedition members decided to have a quick look at the mine dumpings. The air was cool; the African sky was bright blue. Within 10 minutes, Pickford hefted a cantaloupe-sized breccia block and shouted, “Oh, here’s a jaw!”

“All you could see were the side of the jaw and the side of the teeth,” says Conroy. “We knew right away it was a higher primate.” What Conroy couldn’t see were the telltale chewing surfaces of the teeth that distinguish one group of
primates from another. So he set the fossil in a bowl of vinegar to dissolve the breccia. While it fizzled away, four excited scientists speculated.

Judging from a partial root, the canine teeth were too large to have belonged to a prehuman like Australopithecus. From the side, the jaw seemed chimp-like. However, great ape fossils had never surfaced before in Namibia, so Conroy’s group suspected that “Leadbelly,” as they called their creature, was a prehistoric monkey.

About two weeks later, enough breccia had dissolved to reveal the top of one molar. “That was absolutely diagnostic,” says Conroy. “It was not a monkey, but an ape or a human-like ancestor.” More speculation ensued. Van Couvering thought they had a fossil chimp. Pickford bet Conroy a bottle of champagne that Leadbelly was a much older Miocene hominoid.

Leadbelly was the first and last primate fossil found by the expedition. Pickford and Senut returned to Paris to analyze pieces of Leadbelly’s breccia casing. On June 16, they faxed Conroy startling news: Rodent teeth in the rock dated back to the Miocene era. Pickford was right. “It was the best bet I ever lost,” says Conroy.

A Place To Start

Today, Leadbelly is officially known as Otvipithecus namibiensis. Now completely free of its breccia prison, the fossil tells its full story.

The jaw fragment, about three inches long, appears to have belonged to a fully grown animal that died at about age 10 and was approximately two-thirds the size of a mature human. The animal’s dental chart consists of three intact molars, an intact premolar, a partial crown and root for another premolar, sockets for all four incisors, a partial root for one canine tooth and a partial socket for the other canine. While the canine teeth were probably stout, they were smaller than the enormous stabbing canines of the great apes. The incisors were relatively small for a hominoid — a human-like feature. The animal’s tooth enamel, however, probably was thinner than a human’s and, in that respect, ape-like. With teeth like these, Conroy says, Otvipithecus probably ate soft foods like leaves, buds and flowers.

Otvipithecus somewhat resembles Miocene primates found in Europe and East Africa, “but it’s clearly a different animal,” he says. The creature’s presence in Namibia suggests that the region once enjoyed a more temperate climate.
Conroy says *Otavipithecus* could be a candidate for one of two missing links in the evolutionary chain. It may have been a common ancestor to orangutans and the great ape/human family before the two groups diverged about 15 million years ago. Or, as Conroy is more prone to believe, the primate could have preceded the split 10 million years ago between African great apes and the line leading to humans. Conroy says it will take several years to confirm Leadbelly’s place in the fossil record.

However, other paleontologists consider the jawbone promising. “It’s a good starting point,” says Terry Harrison, an associate professor of anthropology at New York University. “The fossil does appear to be close to the ancestry of the great apes and humans. We really need Glenn to find more material.”

The debut of *Otavipithecus* comes at a revolutionary time in paleontology. Some of Conroy’s colleagues are attempting to construct mankind’s family tree by studying DNA mutations in living humans. One group of scientists claims to have worked its way backwards to a literal Eve — an African woman who lived 200,000 years ago. Her genes, the theory goes, are borne by all of us.

Admittedly an old-fashioned bone man, Conroy doesn’t fear professional extinction at the hands of his genetically-oriented counterparts.

“Maybe I’m hopelessly romantic, but you can actually hold the fossil in your hand — hold something that lived 13 million years ago. Holding a test tube... will never replace the thrill of field work.”

“There aren’t enough fossils to go around,” comments John Van Couvering. “Unless you have a bone of your own, you have to shuffle on the sidelines. This discovery puts Glenn on the map.” At the same time, Conroy is preserving the unselfish, collegial spirit of the Namibian expedition, adds Van Couvering. “We all feel very virtuous because it usually degenerates into something nasty. And I would say Glenn is the catalyst. He’s the soul of integrity.”

Conroy says that he, Van Couvering, Pickford and Senut will return to Namibia to search for more otavipithicene fossils, provided he can raise the necessary financial support. In addition, Conroy is organizing a summit of paleontologists next spring at the American Museum of Natural History to discuss Leadbelly and other Miocene hominoids. “It’s rare that the scientists get together to share information,” he says. The main reason hinges on financial and time constraints, but narrow-minded competition also enters the picture. “As I told some colleagues recently, ‘I seek... a kinder, gentler paleoanthropology.’” Thirteen million years after Leadbelly walked the earth, the march of man continues. Conroy at least knows the right direction.

![Martin Pickford (in hat), the paleontologist who picked up the jawbone from the ground, and geologist John Van Couvering at the site in Namibia’s Otavi Mountains where the fossil was located.](image-url)
Stanley Karmeyer, M.D., studies how genetic instructions become garbled and the cancers that are sometimes the result.
Two simple sentences of just a few elements each: “You never lie,” and “I always tell the truth,” illustrate the concept — and the potentially catastrophic effects — of genetic translocation. Switch their components around, and trouble results.
In the hugely complicated world of human genetics, more tangible difficulties occur when chromosomes inappropriately exchange bits of genetic material. Scientists know that at least 125 forms of cancer emerge after chromosomes illegitimately swap genes. The work of Stanley Korsmeyer, M.D., professor of medicine, lies in tracking down the wayward genes that somehow end up out of context after leaving their original sentences and taking up as inappropriate modifiers elsewhere.

Thirty years ago, when the concept that portions of chromosomes could change places was new, researchers had no idea of the number of diseases that would eventually be linked to the translocations. Those are among the benefits of detailed genetic analysis, says Korsmeyer. His laboratory, part of the Howard Hughes Medical Institute, investigates the genetic variations that lead to different forms of leukemia. Using white blood cells from patients with leukemias and lymphomas, the researchers probe for telltale signs of translocated genes, hoping to learn what the genes do and why they break away.

The group recently found several genes that promote T cell acute lymphoblastic leukemia (T-ALL) and follicular B cell lymphoma, two forms of cancer that share a common developmental theme and both tumors involving blood cells. Both are initiated when genes on one chromosome snap off and are appended to DNA on another chromosome. When that happens, all control over the misdirected genes is lost, Korsmeyer says. Despite the seriousness of the problems that arise from these chromosomal translocations, scientists believe they are fairly common. And they are finding them with consistency. For instance, Korsmeyer and other physicians see the same changes in specific tumors time and time again. A child in Africa and a youngster in Arkansas diagnosed with Burkitt’s lymphoma will both have a break between chromosomes eight and 14. A 70-year-old farmer from southern Illinois and a lawyer from Manhattan with follicular lymphoma will have identical exchanges between chromosomes 18 and 14. Certain translocations remain constant despite differences in culture and gene pool, suggesting that they are highly diagnostic.

**Shuffling The Deck**

Scientists believe that leukemias and lymphomas develop partly because the genes in two types of white-blood cells — the so-called B and T cells of the immune system that recognize and destroy viruses, bacteria and other invaders — are at higher risk for translocation than many other genes. That may be because the nature of the work B and T cells do requires gene shuffling. Although they are defined by a small number of genes, B and T cells must respond to a huge number of potential invaders. They accomplish this feat by displaying specialized receptor proteins, called antigen receptors, on their surfaces. Each antigen receptor recognizes only a single invader. In order to deal with the hordes of potential disease-causing agents, B and T cells shuffle the genes that encode their antigen receptors. This gives the immune system a considerable boost, Korsmeyer says, by allowing a few genes to make a large number of products. “If you start with only 52 cards in the deck, the shuffling mechanism allows you to make many different hands by selectively recombining different cards, or DNA segments.”

The shuffling presents a necessary risk. “Without it, your immune system wouldn’t be able to ‘see’ the things — like moon dust — that you’ve never been exposed to before,” Korsmeyer notes. But the shuffling has its price. All that moving around of genes increases the likelihood that some will end up in the wrong place. If all goes well, one DNA segment will join another and the result is beneficial. At times, though, another chromosome might “fly in,” Korsmeyer says, contributing genetic material that is decidedly inappropriate. If that happens, cancer may develop years later, as

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*Graduate students, postdoctoral fellows and research technicians make up the team of scientists in Stanley Korsmeyer’s lab. Standing (left to right): Jennifer Jockel, Zoltan Olvai, Charles Roberts, Lisa Johansen, John Shutter, Diane Merry, Kevin Chow, Peter Domer. Seated (left to right): Curt Milliman, Robert Young, Masahiko Hatano, and Charles Sentman.*
Korsmeyer and other researchers have shown.

T cell acute lymphoblastic leukemia (T-ALL) begins with the alteration of a single T cell. Every cell in the leukemia descends from this common ancestor. Korsmeyer and his colleagues, Masahiko Hatano and Charles Roberts, reported in the journal Science that in T-ALL, a gene from chromosome 10 that normally guides liver growth, called HOX11, is inappropriately shuffled into chromosome 14 DNA in a T cell. The unregulated and out of place HOX11 then helps spawn leukemia by creating legions of descendants of this single abnormal T cell. Putting this volatile growth command into a region of DNA that is very active in T cells ensures the production of millions of copies of this single T cell, Korsmeyer says.

Beyond that, how or why the deregulation happens is not well understood. Identifying other specific fugitive genes, like HOX11, and their specific mechanisms of action has remained a challenging mission.

**Antidote To Cell Death**

For several years, Korsmeyer’s laboratory has been studying another known wayward gene, Bcl-2. Bcl-2 promotes B cell follicular lymphoma, the most common form of malignant lymphoma. Korsmeyer and his colleagues, David Hockenbery, Gabriel Nunez and Timothy McDonnell, recently published several letters in the journal Nature that shed light on the enigmatic dual roles played by many such translocated genes. The articles report that Bcl-2 has a normal role in blocking the programmed death of B cells.

Deploying an army of B cells is part of the immune system’s response when the body is challenged by an invading virus. Once the invader is disposed of and the immediate danger has passed, however, a need remains for the system to stay on guard against the return of the same virus. Bcl-2 blocks the B cell’s built-in death program and allows some members of the well-trained army to survive to fend off a repeat attack, Korsmeyer explains.

Because Bcl-2 is an “antidote to cell death,” Korsmeyer believes it enhances a person’s chance of developing follicular B cell lymphoma. “The longer B cells live, the higher the probability that they will acquire potentially harmful genetic defects,” he says.

Like Bcl-2, other genes being identified as important in producing leukemic blood cells also have normal functions. “They weren’t just inserted into our genome to cause cancer,” Korsmeyer says. For example, HOX11 is a member of a bold family of master genes called homeobox genes. These genes are basically a how-to guide for assembling the body. They make sure that hands become hands and feet become feet, Korsmeyer says. He likens homeobox genes to conductors in an orchestra. “They guide development by switching other genes on and off at precisely the right moments,” he says.

A question that continues to concern scientists is whether misplaced master genes alone are sufficient to cause cancer. A more practical question facing researchers in Korsmeyer’s laboratory is which genes, when translocated, are likely to promote cancer.

Korsmeyer doesn’t yet have all the answers, but the scientists in his lab have identified three new oncogenes: Bcl-2, Ttg-I and HOX11. Using transgenic mice with DNA that has been manipulated to produce a model of each translocation, the group hopes to learn whether translocation alone is enough to cause cancer. These models allow Korsmeyer and others in his lab to study the effect of translocated genes from the moment of fertilization.

Preliminary work shows that Ttg-1, another gene activated in T-ALL, is altered in the embryos of transgenic mice, yet the mice don’t die of T-ALL in utero. They begin to show signs of T-ALL only at about five months. “This tells us that something else has to happen before aggressive leukemia develops,” Korsmeyer says. The “something” might be another internal, genetic event or it might be an environmental trigger that affects cellular life. The body is highly efficient at screening for and destroying mutant cells; it’s only when several damaging events occur together that cancer develops, Korsmeyer says.

Korsmeyer’s most recent results suggest that a single translocation does not appear to be enough to bring about leukemia. “Most cancers are caused by two genetic abnormalities or more. Translocations might be happening all the time at a certain frequency, and it’s the combination of bad luck that’s extremely important in terms of that cell emerging as a malignancy,” he says. It’s as if gene translocations have connotations as well as denotations — only when several suggestions combine does their terrible meaning finally become clear.
The culmination of Washington University School of Medicine's first century was commemorated in many ways: an abundance of social events, an outstanding scientific symposium, the dedication of the new Medical Library and Biomedical Communications Center and a day for family fun at Six Flags. For five days in early October, the medical school community that stretches around the world took time to note the tradition of clinical, educational and scientific excellence that has always been the hallmark of the school. The photographs on these pages represent just a few moments from among the thousands shared by the faculty, staff and friends of the School of Medicine as they reflected upon their institution's reputation and its challenges for the future.

An original play, "Gray's Anatomy: A Medical Fable," was commissioned from playwright Jim Leonard, Jr., and presented at the university's Edison Theater following a dinner at the Hyatt Regency Hotel.
The excitement of the Midwest’s most breathtaking rides and the bonus of no waiting lines filled Six Flags on a day reserved entirely for the faculty and staff of Washington University School of Medicine.

St. Charles County’s Whitmoor Country Club was the site of the four-person scramble Centennial Golf Tournament that attracted some highly skilled golfers — and some duffers — on a beautiful early fall day.

Daniel Nathans, M.D., co-winner of the Nobel Prize in medicine in 1978, returned to the campus of his medical education to preside at one of the scientific sessions presented by eminent scientists from around the globe.

The new School of Medicine Library and Biomedical Communications Center was formally dedicated on Saturday of centennial week. Daniel J. Boorstin, director emeritus of the U.S. Library of Congress, spoke, and tours of the facility were conducted.
C. Everett Koop, M.D., former surgeon general, delivered the keynote remarks at a black tie optional dinner dance held at St. Louis's premiere Adam's Mark Hotel. Koop and former house staff member Robert J. Glaser, M.D., exchanged points of view.

A tour of St. Charles, the oldest city on the Missouri River and Missouri's first capital, was highlighted with stops in Frenchtown and on Antique Row.
Emilie and Theodore Meiners, M.D. '48, (left) and Harriet and John Davidson, M.D. '52, enjoyed conversation in the intimate confines at the top of the Gateway Arch. Their visit occurred during the welcome cocktail buffet held in the Museum of Westward Expansion.

Media — ranging from local television stations to a dedicated edition of the Journal of the American Medical Association — took note of the centennial. Here, Scott Connell, meteorologist for St. Louis' NBC affiliate (KSDK) interviews third-year class president Robert MacDonald.
Guides led a homes and garden tour that featured several mansions in the city's Central West End, Capples House, Tower Grove House and the Climatron and manicured grounds of the Missouri Botanical Garden.

Ann Flipse, daughter of Ann Flipse Gerber, M.D. '59, took a turn at the wheel of the riverboat Spirit of St. Charles during the tour of historic St. Charles.

John B. Watkins, M.D., and his wife Mary enjoyed a dance during a gala evening of cocktails, dinner and dancing at the Adam's Mark Hotel. Watkins recently joined the faculty as a professor of pediatrics and director of ambulatory care at St. Louis Children's Hospital.

During the week of events, celebrants enjoyed lunch under the festive white tent pitched on the medical school's parking lot.
A survey of health care delivery in the United States shows us a system in disarray — one that is unfair, inefficient, confusing, costly and getting worse with each effort at cost control. In spite of spending more per capita than any other country, the United States is 22nd in the world in infant mortality, 24th in the rate of low-birth-weight infants and 12th in life expectancy. Our current system, based on a combination of public health care programs such as Medicaid and predominantly employer-based private health insurance, denies access to care to millions of people and wastes billions of dollars on administrative and billing costs.

The most glaring flaw in

Our current system, based on a combination of public health care programs such as Medicaid and predominantly employer-based private health insurance, denies access to care to millions of people and wastes billions of dollars on administrative and billing costs.

by Patrick S. Clyne, M.D.
our system of health care delivery is the 37 million people without any type of health insurance. Budget crises over the last decade have gutted Medicaid and Medicare until physicians and hospitals are finding that they lose money when they take care of people on public assistance. Uninsured and underinsured people seek medical care at a later stage of a disease process and are less likely to comply with drug treatment and follow-up because of financial concerns. Not only does this adversely affect their health, but the cost per patient rises when care is delayed. The increased cost is borne by all of us through increased hospital and physician charges.

Reform efforts and suggestions have ranged from mandating that minimum health care benefits be provided to all employees to expanding Medicaid and Medicare to provide more benefits. Such patchwork reforms do not address the flaws of the system. It is time to fundamentally change it. In a January 1989 article in the New England Journal of Medicine, Physicians for a National Health Program (PNHP), a new and growing grass roots organization of doctors, outlined a plan to revamp the financing for health care, using Canada’s system as the takeoff point for the proposal, with modifications to fit the U.S.’s unique cultural and political heritage. Under the plan:

- Patients would receive a National Health Program (NHP) card entitling them to care at any hospital or doctor’s office. Patients would not be billed for approved medical care. They would not pay any deductibles, copayments or out-of-pocket costs. All approved costs would be paid by the NHP.
- Most hospitals and nursing homes would remain pri-
care agencies employing salaried doctors and other health care providers would be funded directly from NHP on the basis of a global budget. The NHP would pay pharmacists wholesale cost plus a dispensing fee for prescription drugs on the NHP formulary. Medical equipment would be similarly covered.

We have an opportunity now to demonstrate our commitment to the egalitarian principles that guide our public policy. We need a national health plan to provide equal health care to all Americans. Our future as a just society demands nothing less.

- Private insurance that duplicates NHP coverage would be eliminated, saving an estimated $20 billion a year in industry profits and overhead. Removing the complex and redundant insurance bureaucracy would greatly simplify the paperwork now required of doctors and hospitals, generating billions of dollars of additional savings. More than half of the 18 percent hospitals now pay for administration would be saved under this plan.

The NHP would be funded by redirecting funds now used for employer-based health insurance premiums, copayments and deductibles into the NHP.

Current federal and state payments to Medicaid and Medicare would also go to the NHP.

When fully implemented, the system would provide universal access to everyone. Patient care decisions would be based on need without consideration of the patient’s ability to pay. Technology assessment, resource allocation and community-based social services would be more efficiently assessed and regulated by local planning boards that respond to the local community’s needs. Funds allocated for health care would actually go to providing health care instead of being wasted on excessive billing and administration. Insurance company profits will not add to the nation’s health care costs.

We have an opportunity now to demonstrate our commitment to the egalitarian principles that guide our public policy. We need a national health plan to provide equal health care to all Americans. Our future as a just society demands nothing less.

Editor’s Note: Patrick S. Clyne, M.D., is a resident in pediatrics. Outlook’s editors thank him for the opportunity to publish his opinions.
About four years ago, F.A. Barnett, M.D. ’35, decided to retire. He contracted to sell his family medicine practice in Paris, Missouri, and he and his wife of 54 years, Rita Sue, set out to build a new home in Bella Vista, Arkansas. But events didn’t go as planned. The buyer of the practice, Moberly Regional Medical Center, couldn’t find a physician to operate it. Then, Barnett changed his mind and decided he didn’t really want to retire anyway.

For 53 years, Barnett has provided a source of medical continuity to the 1,400 residents of Paris and many neighboring communities. Out of his office, open seven days a week, he offers an alternative for people who might otherwise drive 26 miles to the nearest emergency room. He sees walk-in patients and those who don’t have a physician as well as those patients who have become fast friends over the years.

Barnett was no stranger to small, rural towns when he moved to Paris in 1938. He grew up in Rocky Comfort, a community of 300 people in the Ozarks of southwestern Missouri. At age 6, he determined that he would become a physician just like “Doctor McCall, who treated me for typhoid fever. I looked upon

Doctor McCall as a boy would look up to a father figure,” Barnett says.

Shortly after his parents separated, with his father remaining on the family’s 120-acre farm just outside Rocky Comfort, his mother moved to town to raise Barnett, his two brothers and his sister. Several years later, as the valedictorian of his high school class, Barnett was the recipient of a Curator’s Scholarship to the University of Missouri. The award covered the cost of tuition.

F.A. Barnett, M.D. ’35, and his wife, Rita Sue. “Without her, I’d never have made it,” Barnett says.

With the country on the brink of depression, many people considered college a luxury. Barnett recalls that family members discouraged him from pursuing a medical career because of the expense involved in the long years of study. Despite their opinion, Barnett says, it was a good time to go to college. “My high-school classmates weren’t earning anything, because there weren’t any jobs. They were marking time and not getting ahead,” he says. Barnett supported himself in college by working part-time jobs. When he transferred to the School of Medicine, he hopped tables at the Timberlake Hotel.

There, he met his wife to be, who was working as a secretary. He and Rita Sue were married on Valentine’s Day, 1937. Between semesters of medical school, Barnett worked in an externship program at Fulton State Hospital. Eventually, he was forced to take out loans to cover the costs of his education.

Of his training at the School of Medicine, Barnett says, “I have nothing but appreciation for the education I received at Washington University. It was the best preparation in my field of study, and I had no excuse but to be excellent.” During his final year, he had the opportunity to work in the laboratory of renowned surgeon and radiologist, Evarts A. Graham, M.D., who had earlier developed the first
successful method for imaging the gallbladder.

When Barnett completed an internship at St. Louis City Hospital, jobs were scarce, but he was hired at Fulton State Hospital. After 16 months there, he learned of a job at the State Hospital. After 16 months, he delivered his own baby girl, a baby boy, was born. Their neighbor, the editor of the local paper, saw him return home. He released the story, which was picked up by the Associated Press and subsequently ran in several newspapers around the country. Barnett says he received many letters from fellow alumni of the School of Medicine who wrote that they would have sent him funds to help cover the cost of a doctor for his wife had they known he lacked the money.

Because Barnett is grateful for the opportunity the School of Medicine gave him to pursue his education, he generously underwrites loans to help needy students. He is a Life Member of the School of Medicine’s Eliot Society. “Because I had to borrow to get through, I wanted to help other needy students,” he says.

Barnett’s commitment and involvement in his community have not gone unnoticed. In 1989, he and his wife received Outstanding Citizenship awards from the Paris Chamber of Commerce, honoring Barnett’s work as mayor from 1957 to 1969 and his wife’s work as chairman of the town’s beautification committee.

During their tenure, Paris built a new high school and a swimming pool, began buying natural gas and switched as architect of the Mark Twain Golf Course, work with the Boy Scouts and the Rotary Club, and contributions as an elder of the Paris Christian Church and as chairman of the Board of Directors of Paris National Bank. Bank president Chuck Brazeale has known Barnett for 15 years. “He’s a real giant of a man,” Brazeale says. “He epitomizes the general practitioner in a rural setting. People know they can count on him. He’s compassionate and caring and sensitive to the family’s well being.”

The Barnett’s son Richard has followed his father’s example. He runs what he describes as a family-medicine cardiology practice in Shreveport, Louisiana, and says it was the inspiration of watching his father work that convinced him to pursue a medical career. He recalls, as a child, accompanying the elder Barnett 30 miles into the country to make a house call. “Today, as a cardiologist, I make house calls,” he says.

F. A. Barnett has enjoyed the steady progression of caring for his patients, their children and their grandchildren. He staunchly believes that children are the most important part of any community.

That is why, in addition to his other philanthropy, he has established a fund to provide five scholarships to members of the Paris High School graduating class each year. The scholarships offer assistance to students during the first year of college.

Of his life serving the members of his community, Barnett says, “Somehow you become part of the family. People really are friendly. We have a wonderful time.” As for retirement, it’s not in his future. After all, things haven’t slowed down much from last year.
Schreiber Named First Flance Scholar

Matthew Schreiber, a second year medical student, has been named the first Flance Medical Scientist Trainee in the school's Medical Scientist Training Program (MSTP).

The newly established scholarship was made possible through a $150,000 gift from the Harry Edison Foundation, an independent organization incorporated in 1949 that supports higher education, social services and medical research.

The scholarship will support Schreiber throughout his MSTP training. After six years of study he will graduate with a combined M.D., Ph.D. degree. A Phi Beta Kappa graduate of Oberlin College, Schreiber received a bachelor's degree in psychology and has had extensive undergraduate research experience.

The award is named in honor of I. Jerome Flance, M.D., clinical professor of internal medicine at the School of Medicine. Flance's association with the School of Medicine spans more than 50 years. He received his undergraduate degree from Washington University in 1931, his medical degree from the School of Medicine in 1935 and has been a member of the faculty since 1942.

Washington University's MSTP, which began in 1968, is the largest MSTP in the United States. The National Institutes of Health has funded 29 programs nationwide.

Directed by Stuart A. Kornfeld, M.D., professor of medicine, the Washington University program offers outstanding medical students an opportunity to train as academic physicians with a background in basic research.

Since 1974, 159 students have graduated from the program, and almost all have gone on to careers in academic research institutions. Of the 75 students who have completed their residencies, 65 are full-time faculty members.

Scholarship Program To Complete First Cycle

Begun in academic year 1989-'90 by the alumni association, the School of Medicine's major merit-based scholarship program is about to complete its first full circle. When four freshmen are named as recipients of the Distinguished Alumni Scholarships next year, four students in each of the school's four current classes will have been awarded the full tuition scholarships.

Funded entirely by annual gifts, the scholarships provide each recipient with $10,000 toward tuition costs. The medical school matches the grant up to the full amount of tuition. Assuming that the students remain in good standing, the scholarships continue for a full four years of education. "The scholarship program helps Washington University School of Medicine compete with other fine medical schools for the nation's very best students," says P. Hannele Haapala, director of annual giving in the office of Medical Alumni and Development Programs.

The scholarships are not based on financial need but on academic merit and the exceptional personal qualities that contribute to the successful practice of medicine. Each of the existing 12 scholarships is named for a distinguished graduate of the school who also is an outstanding member of the faculty. Eugene M. Bricker; Justin O. Cordonnier; Paul O. Hagemann; Alexis F. Hartmann, Sr.; John C. Herweg; Virgil Loeb, Jr.; Carl V. Moore;
Young Scientists Get A Boost

Next summer, five economically disadvantaged high school students will benefit from the foresight of a group of Washington University medical students and the generosity of the medical alumni association. The five high school seniors, to be rigorously selected from St. Louis city schools, will be awarded eight-week, paid positions in medical center laboratories where they will come into intimate contact with lab science.

The medical students see the project — dubbed the Young Scientist Program — as a way to counter a shortage of students interested in the sciences and a dearth of career opportunities for disadvantaged youth. Their proposal was funded for the first year by a $15,000 grant from the Executive Council of the Washington University Medical Center Alumni Association (WUMCAA). "The alumni association is delighted to provide the initial support to a group of students who have taken the initiative and volunteered to serve an important need in the community," says Ira J. Kodner, M.D., president of WUMCAA.

The grant, from association funds, will provide five stipends of $2,000 each and cover support and tracking costs as well. Administrative support will come from the division of biology and biomedical sciences.

Under the program's guidelines, each participant will work closely with a graduate student mentor to complete a short research project related to the participating laboratory's ongoing investigations. A second graduate student will work with the participant on scientific fundamentals. And young scientists will attend weekly faculty-led seminars examining topics such as biological and medical science and career planning in the sciences. At the close of the eight weeks, students will present their findings to an audience composed of their parents and members of the medical center community.

The program, as described by the medical students who designed it, will encourage exploration of research careers, provide support for career decision-making and stimulate interest in science "through active participation while emphasizing close contact with working scientists as role models and advisors."

As part of the agreement to fund the program, the alumni association has asked for a detailed report of the program's success to review after the first year of operation.

Challenge Issued

Asa C. Jones, M.D. '42, and his wife, Dorothy, have offered a $100,000 challenge to all alumni and friends of the School of Medicine to encourage 100 prospective members to join the Medical Eliz'ot Society. Membership in the society is bestowed upon those who contribute $1,000 or more to current priorities at the medical school.

The challenge was announced and received with applause at the September 16 meeting of the School of Medicine Eliot Society Membership Committee, co-chaired by Nicholas T. Kouchounos, M.D. '61, and Phillip E. Korenblat, M.D., former house staff.

The challenge remains in effect until December 1992 and promises to match the gifts of new Medical Eliot Society members up to a total of $100,000. The Jones' gifts will go to the Department of Orthopedic Surgery.

Alumni and friends of the medical school are invited to contact the school's development office at (314) 362-8273 to learn more about the Asa C. and Dorothy W. Jones Challenge Fund of Washington University School of Medicine.
Mordecai P. Blaustein, M.D. '61, heads a team of researchers that has developed a test for determining levels of ouabain in the blood. According to the research, abnormal amounts of ouabain might characterize individuals likely to develop high blood pressure. The substance has been implicated as a possible cause in a high percentage of people with hypertension. Interestingly, the hormone is structurally and biologically identical to a substance from plants that South American Indians once used as a poison on the tips of their arrows. Blaustein and his colleagues reported their findings on this human endogenous digitalis to the American Heart Association for High Blood Pressure at its 44th annual conference.

Donald A. Hazlett, M.D. '67, recently retired from the U.S. Navy after 21 years of service. He currently is in the private practice of psychiatry and serves as medical director for Clarion Psychiatric Center, a 52-bed free-standing psychiatric hospital in Clarion, PA. He and his wife, a school nurse and a graduate student at Slippery Rock University, have three children ranging from 22 to 5 years of age.

Donald R. Kirks, M.D. '68, has recently had the second edition of his textbook, Practical Pediatric Imaging: Diagnostic Radiology of Infants and Children, published by Little, Brown and Company. The first edition sold more than 6,000 copies and was recently voted the most popular textbook of pediatric radiology by residents in diagnostic radiology and diagnostic radiology residency program directors. Kirks is director of the Department of Radiology at Children's Hospital Medical Center in Cincinnati.

David Stabenow, M.D. '68, has been promoted to brigadier general in the U.S. Army Reserves. He was called to active duty during the gulf war and served as deputy commander of Brooke Army Medical Center in San Antonio, TX. He is now back in the private practice of dermatology in Dubuque, IA.

is the founder and director of the Geriatric Consultation Center in New York and the director of the Department of Gerontology at the Staten Island University Hospital. He lives in New York City and East Hampton with his wife, a son and a daughter.

60s

Jerome M. Aronberg, M.D. '71, passed his private pilot test in July, 1991, and is now working on an instrument rating.

Robert F. Scheible, M.D. '72, has been named as a fellow of the American College of Radiology. Selected for his outstanding contributions to the field of radiology, Scheible was named one of 129 new fellows by the college's board of chancellors. Criteria for selection include performance of outstanding service as a teacher of radiology, service to organized medicine and an outstanding reputation among colleagues and the local community.

Eugene C. Rich, M.D. '77, director of the University of Kentucky Medical Center's division of general internal medicine and geriatrics, is among the first 18 health care leaders to complete a Primary Care Policy Fellowship sponsored by the U.S. Public Health Service. In the intensive workshops, participants considered the future of primary health care in the United States. Fellows met with Louis Sullivan, M.D., secretary of the Department of Health and Human Services, and with key Congressional staffs.

80s

Pamela R. Edmonds, M.D. '80, of Ardmore, PA, became an associate professor at the Medical College of Pennsylvania in October, 1991. She and her husband are raising Michael, 4, and Sara, 2.


Clifford V. Harding, III, M.D., Ph.D. '85, has been named a 1991 Pfizer Scholar. The award of $65,000 annually for two years goes to outstanding physicians who have finished clinical and research training and assumed full-time faculty status at a U.S. medical school. Harding studies the molecular and cellular mechanisms of antigen processing here at Washington University. Presenting the award was John E. Jeffers, M.D., of Pfizer, Inc.

Janice Rha, M.D. '88, was married to Brian Egan, CPA, on July 6, 1991. The couple resides in Redondo Beach, CA.

Ellen Reynolds, M.D. '89, is completing her second year of residency in general surgery at Massachusetts General Hospital and is excited to announce her marriage to Ray Launer.

Gene L. Davis, M.D., F.H.S. '73-'76, has recently completed a Master's Degree in business administration at Webster University in St. Louis. He has also been elected to fellowship in the American College of Radiology.

Jo Havenner Ellerbrake, P.T. '57, executive director of the Ranken Jordan Children's Rehabilitation Center in St. Louis County, received the 1989 Women of Achievement Award for Health. Sponsored by local media, the award recognizes women who have made outstanding contributions to the St. Louis community. Ellerbrake speaks regularly on the topics of maternal and child health, lead intoxication and pediatric brain injury.

Mrs. Carl Yochum, P.T. '59, reports that she was honored with Christian Health Services President's Award for 1991 for "quality service, dedication to the organization, leadership ability and loyalty to staff."

Jane Hall, P.T. '84, recently completed a Masters of Science in sports physical therapy and athletic training at the University Of North Carolina, Chapel Hill. She currently practices at a sports medicine clinic in Cupertino, CA, and is establishing a cycling injury evaluation program.

Cindy Ringel-Williams, P.T. '84, and her husband announce the birth of their third child, Blaire Marie, born in January 1991. The family resides in Mt. Hope, WV.

John M. Fraser, H.A. '78, is the new chief operating officer of Methodist Hospital in Omaha, NE. Fraser previously served as senior vice president for medical and professional services at St. Luke's Episcopal Hospital in Houston.

Dale S. St. Arnold, H.A. '86, recently was appointed an executive vice president of Mount Carmel Health and chief operating officer of the 287-bed Mount Carmel East Hospital in Columbus, OH.

Gregory A. Walters, H.A. '86, and his wife, Jane, announce the birth of Lindsey Rae, born December 21, 1990, in Greensboro, NC. Lindsey makes four in the Walters family, including her older sister Katherine.
A party at the home (and orchid greenhouse) of Ira J. Kodner, M.D., president of the Washington University Medical Center Alumni Association, welcomed new medical students to St. Louis during the warmer days of August 1991.
On Sunday, October 13, members of the medical school community enjoyed a day at Six Flags as an exuberant finale to the week-long celebration of the school's first 100 years. For a more complete record of celebration activities, see the collection of photographs in this issue.