Outwitting sudden cardiac death
A small, vellum-bound book rests on a page of marbled paper — both from the Washington University Medical Library's collection of rare books. See page 8.
The Wisdom of the Ages 8
Both beautiful and informative, medical texts from centuries ago are preserved in the library.

The Switch, the Pump and the Blip 14
Thalassemia patients get help and hope for their genetic disease.

Keeping the Beat 18
Sudden cardiac death is revealed as an electrical problem.

Our Fair Quota: The Nobel Spirit 22
The medical school’s Nobel laureates exert a broad influence.

Newsbriefs 2
Student Stage 27
Silhouette 28
Alumni Report 30

On the Cover:
An artist’s vision depicts the disruption of the heart’s rhythm that leads to sudden cardiac death. Illustration by R.G. Michaels.
Allergist's Advice Could Put Cats In A Lather

Spilsh splash, give your cat a bath. That's the advice researchers are extending to legions of cat owners who are allergic to their pets but refuse to part with them.

When it comes to relieving allergic reactions to cats, a monthly bath may be far more effective — and certainly less expensive — than the drugs and shots upon which most cat-sensitive patients currently must rely, says allergist H. James Wedner, M.D., associate professor of medicine. Wedner directed a team of researchers who presented the simple method for reducing cat allergenicity at the American Academy of Allergy and Immunology's annual meeting, held in Baltimore.

A monthly 10-minute washing in lukewarm, distilled water markedly reduced the production of Fel D1, the major allergen in cats, the Washington University researchers reported.

Jazz, the shop cat at the Salty Dog grooming service of Robert and Pam Bolton, doesn't mind a bath, despite his look. The Bolton's regularly bathe about 20 cats and say the animals learn to like the procedure.

In a study of 10 cats, they found a consistent decrease in Fel D1 production beginning in one cat after three washes and in all 10 cats after seven washes. The amount of Fel D1 each cat produced varied, but the average decreased from 3,031 milliunits per cat at wash one to 400 milliunits per cat at wash nine.

Fel D1, a protein produced by the salivary and sebaceous glands, is deposited on the skin and hair either as the hair passes through the sebaceous gland or as the cat preens. It is a major component of the cat dander that is ubiquitous in cat owners' homes.

Wedner and his colleagues are unable to explain why monthly washing decreases production of the allergen. "While the washing procedure might be expected to alter the skin production of Fel D1, we wouldn't expect it to have a significant effect on salivary production," he says. "Washing is effective, however, and that suggests the skin may contribute more to overall Fel D1 production than was previously thought."

Regardless, he comments, any strategy to reduce production of Fel D1 would, by decreasing its prevalence in the environment, decrease symptoms and suffering for cat-sensitive patients.

As to sheer numbers of cat-sensitive patients, there seem to be no exact figures. According to the American Academy of Allergy and Immunology, some 10 percent of the general population — and 20-30 percent of asthma patients — may be allergic to animals. And though nobody knows why,
cats are more likely than dogs to cause allergic reactions.

Cats are currently the most popular pet in the United States, and cat ownership seems to be on the upswing, reports the Washington, D.C.-based Pet Food Institute. Cats reside in 30 percent of the 92.5 million homes in this country, the institute notes. According to its figures, that translates to 57.9 million felines.

Would monthly bathing create, well, a catwaif? Probably not, says the American Veterinary Medical Association (AVMA).

While cat washing may not be regular practice, it’s not that uncommon, says AVMA spokesperson Sharon Curtis. “You always hear that cats take care of themselves, but I’ve been hearing more and more about people who do wash their cats.” As far as the actual bath, reactions will vary depending on the age of the cats — the younger they are, the easier they adapt — and temperament. Curtis recommends consulting a veterinarian for advice about shampoos, if they are to be used, since cats can be allergic to certain chemicals. She notes also that a vet may suggest tips for easing cats into the bathing routine.

“In our study, cat washes were performed under light anesthesia,” Wedner says. “Cats can, however, be trained to accept bathing as a standard procedure, and this is particularly easy to accomplish in kittens. Bathing is not harmful to them and, in fact, show cats and some exotic breeds require frequent bathing.”

### New Medical Imaging System Under Development

Art and science overlap in a laboratory in the Clinical Sciences Research Building where a sensing system first conceived and built as a high-tech method for producing fine portrait sculpture is being adapted to serve the goals of medicine. According to Michael W. Vannier, M.D., professor of radiology at Washington University’s Mallinckrodt Institute of Radiology, the equipment promises to become a “brand new tool for biomedical imaging.” And he says that locating the machine was “quite a find.”

Bearing the name Cencit after the firm that first developed the technology to carve busts using a computer-driven machine tool, the device collects a complete set of descriptive data for any surface placed within its dome-shaped chamber. The dome comfortably accommodates a seated person.

Earlier methods for gathering three-dimensional data required 15 to 90 seconds to do their work; Cencit needs only about three-quarters of a second. In an eyelink, six cameras and six flash tube-powered projectors mounted in the dome combine to triangulate every point on a surface. Each complete dataset consists of 144 frames and requires nine megabytes, or 9 million characters, of computer storage.

Complicated computer algorithms then interpret the data from the specialized video cameras and recreate an accurate three-dimensional image. Rather than transmit that information to produce statues, Vannier and his colleagues work with computer-graphics images and color hard copy as a final product. Adding analysis software and carefully calibrating the system makes precise measurement of any surface detail possible. “We can record the surface of the body or any part of the body in a fraction of a second,” says Vannier.

For the physician, such a tool will relate external landmarks to internal anatomy, facilitating the accurate guidance of biopsies or the positioning of patients for other scanning procedures with up-to-the-second information. For the reconstructive surgeon, a no-risk method for gathering precise physical descriptions may prove invaluable. With no anesthesia required and no ionizing radiation involved, the speedy imaging device may one day find a large place in the practice of pediatrics as well.

“A big literature on the mathematical description of surfaces exists,” says Vannier, “but there are very few tools for doing the work.” The Cencit device at the School of Medicine is one of four in the world; two remain at the parent company, a subsidiary of St. Louis-based CPI Corporation, and the other is in the hands of the U.S. Army as a tool for guiding the precise fit of gas masks to the faces of its personnel.

Collaborating with Vannier on projects to develop the scanner as a medical tool are co-investigator Leroy V. Young, M.D., professor of plastic surgery, and research engineer Gulab Bhatia, one of the machine’s developers. The researchers are working toward manipulating images more quickly, and Bhatia has written software that allows the processing of the data to include precise quantitative measurements. A protocol also is underway to assess the tool’s efficacy as an aid to surgical procedures involving the face and head. With the project only four months old, the team already is producing high quality hard copy. “We are committed to developing an effective tool,” Vannier says.

The project is funded in part under the Missouri Research Assistance Act, which states as its goal, “to promote research projects and applied projects which will enhance employment opportunity in Missouri, stimulate economic development and encourage private investment.” Also contributing funding are the Cencit Corporation and Washington University.
Study Shows Best Treatment For Advanced Breast Cancer

Although a larger percentage of breast cancer is being diagnosed early, when treatment is most effective, for those women with locally advanced breast cancer — what physicians call stage III — the best approach now appears to be a combination of three regimens: radiation therapy, chemotherapy and surgery. According to recent research at the School of Medicine, the sequence in which the individual treatments are prescribed also may be vitally important to success.

In their study of 237 women treated with various combinations of the three approaches over a span of 20 years (1968-1987), Mary V. Graham, M.D., and her colleagues in the Radiation Oncology Center at Mallinckrodt Institute of Radiology report that survival rates were significantly higher when all three treatment options were combined. Local control of tumors — prevention of recurrence at the original disease site — also peaked when systemic therapy, irradiation and mastectomy were combined.

Though mastectomy alone has been shown to yield poor results, with relapse rates as high as 78 percent five years after the surgery, Graham says "mastectomy is important for local control of tumors, even though the movement in general has been away from it. Sometimes, the tumor burden is apparently just too great for alternative therapies." An instructor in radiation oncology, Graham presented the results of her study to the annual meeting of the American Society for Therapeutic Radiology and Oncology, held in Miami Beach in October, 1990.

All of the subjects in the retrospective study were diagnosed as having stage III disease, one of four classes to which physicians assign all breast cancers. Stage III is characterized by a tumor five centimeters in diameter or larger, with skin or chest-wall involvement or advanced lymph-node disease.

In stage I cancer, the tumor is less than two centimeters in diameter, with no lymph-node involvement and no distant metastasis, or shifting of the disease. Stage II comprises disease with tumors as large as five centimeters or lymph-node involvement. And stage IV displays metastases to distant sites in the body.

According to Carlos A. Perez, M.D., director of the Radiation Oncology Center and a collaborator on the research, a smaller and smaller percentage of women with breast cancer is being diagnosed with advanced disease — either stage III or stage IV. "Thanks to screening mammography, public awareness and physician education, early diagnosis is becoming more common," he says. Still, of the one in 10 women who will be afflicted with breast cancer, perhaps 20 percent will be diagnosed with advanced disease.

"Many of these are neglected cases — women who did not seek medical attention for whatever reason. And some just have aggressive tumors that are not diagnosed until they are more advanced," says Graham.

The authors also report on how successful the four treatment modalities were in controlling recurrence of cancer at the original site five years post-treatment. The success rates: 31 percent — irradiation alone, 47 percent — irradiation and systemic therapy, 80 percent — irradiation and mastectomy, and 93 percent — irradiation, mastectomy and systemic therapy combined.

The investigators also examined the effectiveness of the treatment when the sequence of its various elements was taken into account. They divided those women who received all three therapies into two groups: one that received mastectomy prior to getting systemic medication and irradiation therapy (in the conventional order), and another that began chemotherapy and/or radiation therapy before undergoing surgery (a less traditional approach).

Although the results were not statistically significant, Graham reports an increase in survival rates for women who were treated with chemotherapy and/or radiation before they underwent breast surgery. "It may be that success depends upon not just what treatment we give, but when," says Graham.

Perez speculates that the better survival rate seen when the traditional order of therapies is reversed may be due...
First Monsanto Scholar Named

Roderick L. McCoy

Roderick L. McCoy first learned of the Washington University Medical Scientist Training Program (MSTP) when he was a high school student in Santa Monica, California, and as he says, "trying to decide what to do with my life." Today, he is a second-year student in the School of Medicine and the first Monsanto Scholar in the newly established Monsanto Scholars-Medical Scientist Training Program for Minority Students.

The award — made possible through a $600,000 gift from the Monsanto Fund — will enable McCoy and students selected in future years to receive paid tuition and a monthly stipend while pursuing combined M.D. and Ph.D. degrees in the rigorous six-year program. Monsanto Scholars will be named annually, with the program supporting as many as six students at a time. The Monsanto Fund is the philanthropic branch of Monsanto Co.

"Vitaliy needed improvements in health demand that we attract the most outstanding young scholars of all backgrounds to careers in biomedical research," says William A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine. "We are extremely grateful to the Monsanto Fund for providing Washington University School of Medicine with a unique opportunity to address this goal."

McCoy is a graduate of Stanford University, where he majored in electrical engineering and built a strong science background. He plans to pursue a growing interest in immunology and currently works in the laboratory of immunologist Dennis Loh, M.D., as part of his six years of MSTP training.

Directed by Carl Frieden, Ph.D., professor of biochemistry and molecular biophysics, the MSTP began at Washington University in 1968 and is one of 29 nationwide funded by the National Institutes of Health (NIH). The program offers outstanding students an opportunity to train as academic physicians with a background in basic research. "This is an important program for the medical and graduate schools," says Frieden. "It attracts outstanding students who have an interest in research and medicine." The Monsanto Scholars program is a way to attract minority students to the medical field, he adds. At present, four minority students are enrolled in the MSTP.

Washington University operates the largest MSTP in the United States. Since 1974, 148 students have graduated from the program and the great majority have gone on to careers in academic or research institutions. Of the 72 students who have completed 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.

Monsanto will contribute more than $17.5 million to communities worldwide in 1990 through the Monsanto Fund and other contribution programs operated by the corporation and its subsidiaries. More than $5 million of that total will be directed to educational programs at colleges, universities, public high schools and elementary schools. "Education and science education especially, has been our priority emphasis during the 1980s. And it continues to be our major interest area into the 1990s," says Mason.
Attention To Detail: Watching The Brain Pick and Choose

Have you ever walked into a crowded room and spotted a friend by recognizing his favorite red sweater? Maybe you picked him out because he’s tall or because of the way his shoulders move when he walks. Whether it was his sweater, his height or the sway of his shoulders, you paid attention to a particular type of visual information.

The search shifted your visual system into high gear and a remarkable process of elimination allowed you to sift through your surroundings and select what you needed to find that familiar face.

This amazing ability of the brain to select the information it needs and bypass what it does not has interested scientists for years. Only recently have the tools and knowledge become available to explore the recesses of the brain where these routine functions take place.

At Washington University School of Medicine, scientists have used PET (positron emission tomography) to observe activity in the brain’s regions of the brain that are related to different aspects of visual objects, like color or shape or velocity. We wanted to identify areas related to those things. Then we wanted to see if we could show what effect attention has on those areas by manipulating what people do with the visual stimulus. Rather than manipulate what went into the eyeball, we manipulated what study techniques people were thinking about.”

“Different stimuli activate different areas of the brain,” says Corbetta. “If a stimulus such as color is being attended to, the frequency of neuronal firing increases in a specific region of the brain.” At different times, subjects were asked to identify changes in a single characteristic and changes in all three characteristics. Subjects proved to be more sensitive to subtle changes when they focused on a single characteristic, Petersen says, which shows, “You do better looking for one thing than looking for several.”

“Even though the visual stimuli were the same, when you pay attention to a particular characteristic such as shape, what you are thinking about turns up a certain visual association area,” he explains. “We actually could measure what people were thinking with PET, because the scan or exposure picks up how the marker is flowing through the brain. Blood flow changes locally with how hard your brain is working — how much nerve cells are firing.”

“If you’re told to look in a crowd for a friend wearing a red coat, looking for the redness helps you find your friend,” he says. “You are given that information and are able to use it.”

Maynard V. Olson, Ph.D., was among the participants in the symposium, “Genome Analysis at Washington University,” sponsored by the Center for Genetics in Medicine. The symposium’s various speakers explained their work in lay terms and related it to the recently funded Human Genome Project. The School of Medicine is one of four centers of investigation in the initiative that will eventually decipher the complete genetic message of human beings.
Scientists are just beginning to understand attention, he comments. One reason it has captivated the scientific audience is because it is the cornerstone of consciousness.

"Studying attention is a way to get close to studying consciousness," Petersen says. "It is studied a great deal in the fields of psychology, philosophy and neuroscience — all are interested in attention because it's so relative to how we interact with the world. It's of great interest to curious humans in getting closer to understanding how we become conscious human beings.

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**Patient Cured of Abnormal Heart Rhythm**

A 46-year-old Illinois woman is among the first patients in the nation and the first in Missouri to be cured of an abnormal heart rhythm using high-frequency, electrical energy.

The patient was discharged from Barnes Hospital on Oct. 24. Doctors here say the new technology may eliminate the need for medicine or surgery in many patients with certain types of heart rhythm abnormalities.

The technique, called radiofrequency catheter ablation, is being studied at the School of Medicine under the direction of Bruce Lindsay, M.D., Robert Hoyt, M.D., and Michael Cain, M.D.

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**Waterston Receives $3.8 Million From NIH**

*Robert H. Waterston, M.D., Ph.D., professor of genetics and associate professor of anatomy and neurobiology, has received a $3.8 million grant to develop large scale DNA sequencing methods.*

The three-year award comes from the National Institutes of Health's (NIH) Center for Human Genome Research. It supports in part the collaborative effort between Waterston's group at the School of Medicine and the group of John Sulston and Alan Coulson at the Medical Research Council (MRC) Laboratory of Molecular Biology in Cambridge, England. The MRC will provide $1.9 million in funding.

The three-year project will begin sequencing the complete genetic material (DNA) of the C. elegans nematode, a tiny transparent worm. This animal is an important model for studying development and cell biology worldwide. The project's aim is to sequence 3 million base pairs or, 3 percent, of the entire DNA of the nematode. If successful in this initial endeavor, the groups will expand their efforts to tackle the entire sequence. The project also involves evaluating the effectiveness of currently available automated sequencers in large scale DNA sequencing and developing computer software to aid in handling and interpreting the large amounts of data that such a project entails.

Waterston has worked in recent years on the construction of the physical map of the worm's DNA, which serves as the basis for the sequencing project. He also is recognized for his genetic research involving muscle development in the nematode and recently received MERIT status from the NIH to continue that work.

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

A 1965 graduate of Princeton University, Waterston received his M.D. and Ph.D. in 1972 from the University of Chicago. He served his internship in pediatric medicine at Children's Hospital Medical Center in Boston and was an American Cancer Society and Muscular Dystrophy Association post-doctoral fellow at the MRC Laboratory of Molecular Biology in Cambridge. He joined the School of Medicine faculty in 1976. He returned to Cambridge as a Guggenheim Fellow in 1985 for a sabbatical year.
The WISDOM of the Ages

By Kleila Carlson

An ornamental initial capital from Andreas Vesalius' De Fabrica (1543), considered the most beautiful textbook ever printed.

One is a jewel

out of the past by Paracelsus, a spirited and fanatical scientist whose primary interest was treatment of open wounds, but who, according to one report, was unable to save himself from dying of such an injury in a tavern brawl. (In fact, he more likely succumbed to a stroke.) Another features Georg Bartisch, who began as a barber's apprentice and became a noted authority on surgery and ophthalmology. Offering insight into a quasi-scientific kind of medicine that once provided a roundtable for musicians, magicians, philosophers and astronomers, they are the rare texts — some as old as 500 years — of the Washington University Medical Library's archives and rare books division.

Photographs by Tom Heine
This watercolor from 1617 was found on the interior cover of the original boards of a work by Robert Fludd, an "astrologic physician." It depicts the medical philosophy of materialistic pantheism—that man is the world in miniature, with all the parts of both corresponding and acting upon one another.
More than 5,000 rare volumes are in three collections recently acquired from the library of the St. Louis Metropolitan Medical Society. The medical society, the oldest of its kind west of the Mississippi River, closed its own library earlier this year. The School of Dental Medicine transferred approximately 1,000 volumes, including a second edition of Zene Artzney (1532) which is reported to be the first book ever devoted strictly to western dental therapeutics. Until the volume was cataloged here, no copy was known to exist in North America.

Probably the most significant collection from the medical society is that of Robert Schlueter, M.D., a St. Louis physician who lived from 1872-1955. Schlueter's Paracelsus collection is considered the world's largest library of works by or concerning the German renaissance physician and philosopher Philippus Aureolus Theophrastus Bombast van Hohenheim, who was known as Paracelsus. Perhaps the most original medical thinker of the 16th century, Paracelsus was a controversial figure who advanced medicine by quarreling about it. He has remained controversial for five centuries, with a lasting effect on the development of western thought. The Schlueter Collection includes more than 400 titles dating from 1530 to 1970.

The James Moores Ball Collection, rich in anatomical atlases dating from the 16th to the 18th centuries, reflects the interests underlying Ball's scholarship as exemplified by his biography of Andreas Versalius and by his study of the practice of body snatching. A St. Louis physician who died in 1929, Ball was an avid bibliophile and eminent member of the St. Louis Medical Society. Approximately 400 titles compose his collection.

The General Rare Books Collection from the St. Louis Metropolitan Medical Society is a composite of more than 3,100 acquisitions and gifts, from a 1569 text on herbal treatments to early 20th century works. It also includes a 1681
work by Francois Mauriceau, who is credited with establishing obstetrics as a separate science.

The Henry J. McKellops Collection was the historical gem of the School of Dental Medicine. McKellops, a recognized leader in the profession of dentistry and an early St. Louis practitioner, helped organize the Missouri State Dental Association and was its first president. Among his volumes are 18th and 19th century titles in French and German, as well as works by early British and American medical authors.

Susan Alon, rare books librarian, says in recent months the library has amassed works it normally would have taken years to collect. Managing the collection is a challenge that both overwhelms and excites Alon, who herself is a newcomer to the library.

"I would like to have this be a must-see for doctors bringing visitors to the school and medical center," says Alon, who was at the Yale Medical Historical Library for 12 years before coming to Washington University last April. "This rare books collection is one thing that

(Above) The anatomical plates of Pietro Berretini were lost for more than a century, having been engraved in 1618 and not published until 1741. Berretini's figures are often representations of entire bodies in action, such as this gracefully gesturing figure set in a traditional renaissance landscape.

(Left) William Cowper's Myotomia reformata is among the most beautiful atlases of the 18th century, employing a fluid style of artistic anatomy in its copperplates, some after Rubens and Raphael.

(Top right) From Jean Galbert Salvage's Anatomie du gladiateur combattant (1812), this classic copperplate engraving representing the bones and muscles of the head and neck is an excellent example of the intersection of art and anatomy.
IVLII CASSERII PLACENTINI PHILOSOPHI ATQ MEDICI PATAVII
VTRANOVE MEDICINAM EXERCENTIS
DE VOCIS AUDITVSO ORGANIS
HISTORIA ANATOMICA
SINGULARI FIDE METHODO AC INDUSTRIA CONCI\NATA
TRACTATIBVS DVOVBS EXPLICATA
AC VARIIS ICONIBVS
ÆÆÆÆÆÆÆÆÆÆ
ILLVS
TRA
TA
The oldest book in the collection, the 1477 treatise Arzneibuch, by Ortloff von Beylandt. To a large extent, its format is based on that of the medieval manuscript.

distinguishes this medical school from others. There are few of these collections, probably fewer than a dozen significant collections in the country, but there are many medical schools.

On the seventh floor of the library, highlights of the collections are prominently displayed in glass cases along the outer corridor of the archives and rare books division. There, the browser can view first and second editions of Georg Bartisch's writings on eye treatments, the first work of its kind written in German; a first edition of Opera chirurgica (1564) by Ambrose Pare, a skilled surgeon who was considered the authority on the subject in his day, and a first edition (1569) of Girolamo Mercuriale's work on the benefits of exercise and medicinal hot baths.

Works not on display are stored in a humidity-controlled vault or shelved in an adjacent area while they await cataloging. Alon predicts the task of defining the collection for some time as she determines what is valuable and what is merely old. The Homcrest Foundation, a private charitable enterprise in New York, has provided a three-year grant to conserve and catalog the collections.

Although some volumes are in disrepair, most of the works have withstood the test of several centuries well. Many of the books are printed on cotton rag paper and bound with vellum or parchment, durable materials that increase their longevity. "These books are in better condition after 500 years than books produced much later," Alon says. The detail of the illustrations contained in the texts also indicates the high quality of the collections. In many instances, lengthy collaboration between anatomist, engraver and printer meant that producing a single chapter required three to four years. Alon says the illuminations would compare favorably with any modern anatomy book's illustration.

No total dollar value has been placed on the rare books collection, but in many instances the worth of a single volume exceeds the library's $10,000 annual book budget. "It is a significant resource for this mid-continental region," Alon says. On the average, two to five rare books are added each year.

More important than their monetary value is the books' great research value and their contribution to the study of medicine today. "The history of medicine is so important to the study of medicine that it is an integral part of it," she says. "You would be surprised at some of the information contained in these older medical texts."

Paul G. Anderson, Ph.D., who heads the archives and rare books division, says the recently acquired collections have fortified the library's already strong areas of ophthalmology, obstetrics and midwifery, brain localization and function and deaf education. With the acquisitions, he hopes to satisfy both current researchers and those looking at medicine from a totally historical perspective. "Collections such as these make one aware of all sorts of values that were important to a particular time," he says.

Looking at obstetrics in the 17th century, we’re able to infer attitudes about women, family and children. The same is true of warfare, battles and politics if we read about the healing of wounds. Attitudes toward mental health can be inferred by knowing more about the notions of witchcraft and medicine.

Though the history of medicine is very specific, Alon stresses that it is also "very interdisciplinary," because prior to the mid-19th century medicine was not as specialized as it is today. "Everybody had a philosophy of health and everybody contributed to the discussion," she says. "Medicine was caught up in music, magic, philosophy and astronomy. Regardless of your subject or field of research, I can find something in the history of medicine that will have an important bearing and be of interest to your research."

Both Alon and Anderson hope the collections will be of interest to faculty and staff at the hilltop campus as well as the medical school.

"A collection only comes alive when people use it," says Alon. "Knowledge of the collection grows as researchers use it. A collection is quiescent, which this one is, because of lack of use."

The last large collection contributed to the rare book holdings came in 1977 when Central Institute for the Deaf donated its library on otology and deaf education assembled by its founder, Max Aaron Goldstein, M.D. The rare books division was established independently from the archives in 1974 and contains more than 16,000 volumes. □

A representative and emblematic title page is from Casserius' De vocis auditus organis historia anatomica (1600). The illustrations contained in the text include the first drawing of a human tracheotomy, without anesthesia.
The Switch, The Pump & The Blip
Life with Thalassemia
by Steve Kobler
When Chris Tsangaris was just three months old, a carefully timed genetic switch closed deep inside the red blood cells of his infant body. Without so much as a click, the mechanism turned off specific fetal genes and activated their adult counterparts. The switch — common to us all — worked fine. But the newly activated genes did not. And that has made all the difference for Chris Tsangaris and the millions like him whose lives are ravaged and shortened by the genetic disease called thalassemia major.

As a result, Chris’ bone marrow, where red blood cells develop, began to struggle and swell in a futile attempt to make enough hemoglobin to do the oxygen-carrying job. His bones became thin and brittle. The ineffective hemoglobin damaged any normal red blood cells that were being produced, and a dangerous anemia plagued him.

The course of treatment: regular blood transfusions. From the age of three months, Chris got new, oxygen-rich blood twice every month. Now, at 34, he’s had perhaps 750 transfusions. For thalassemia major patients, there is no option. Without transfusions, death is a near certainty before the age of five.

Transfused blood brings a reprieve, but it also carries its own cost in the form of a heavy load of iron that cannot be removed. Chris’ physician, Timothy Ley, M.D., explains: “Thanks to transfusion, the marrow gets the message that enough red blood cells are present and backs off. Bony defects become less severe and the anemia is alleviated. Life becomes relatively normal until a patient reaches his mid-teens. Then iron loading begins to cause problems.”

Most thalassemia patients require two units of blood every month, each of which contains 200 milligrams of iron. A normal daily intake is a single milligram. The simplest math shows the thalassemia patient’s monthly dose of iron to be about 13 times normal. “The body is designed to hoard iron, not to eliminate it,” says Ley, a hematologist. Faced with such huge quantities, the system soon shunts the overload into tissue where it does not belong.

Endocrine organs take a share of the excess, with the result that growth and sexual development are arrested. The liver suffers. Often, as in Chris’ case, diabetes sets in when the pancreatic islets are poisoned by iron. The skin takes on a dark, bronze hue. And most dangerous of all, the muscle cells of the heart are damaged. If the iron loading goes unchecked, thalassemia patients receiving regular transfusions almost all die before their 20th birthdays, Ley says. Most often, the cause is heart disease. Transfusions alone, therefore, are only a delay, an imperfect treatment that eventually fails.

Eliminating the iron is the second, equally vital, half of the therapy. Ley, an associate professor of medicine who has studied thalassemia for his entire career at the School of Medicine and before that at the National Institutes of Health, says that removing the iron is an attainable goal. For 15 years, the drug Desferal has been employed as an iron chelator — a chemical compound that binds iron into a ring within its own molecular structure. Because Desferal is soluble, the body secretes it, and with it goes the undesirable iron.

Not a perfect therapy, Desferal has an active half-life of only about 10 minutes, so oral administration or shots are not useful. Instead, patients wear computer-controlled pumps that deliver subcutaneous or intravenous doses over a long period. Usually, the treatment requires six days of medication out of every seven, with the pump — carried on the belt or in a hip pocket — running for 12 hours each day. Sunday is a day of rest.

Though not restrictive, the pump creates a certain presence in a young person’s life that may be resisted or even rejected. Chris Tsangaris has made it his life’s work to “get kids to pump,” as he puts it. He travels internationally, organizing and speaking about the needs of thalassemics; he visits families and gives demonstrations for newly diagnosed patients and their apprehensive loved ones; and he’ll show his own pump and catheter to anyone who expresses an interest in thalassemia. “The public doesn’t know, and they should,” he says. Chris’ list of service to the Thalassemia International Federation (TIF), the Cooley’s Anemia Foundation and the
Thalassemia Action Group (TAG) includes ex-presidencies, regional directorships and enough one-on-one experiences to shame a Larry King. He knows the needs and fears of the thalassemic as only another can. The people who are his family as much as any kin could ever be, he calls "the patients."

His best friend, a patient in Boston, is giving a benefit dance to raise funds for the treatment of someone who can't afford it. Chris will fly there. He says: "All the patients go. We get together; we talk about our world, and we get strong. Conferences and get-togethers are the best things that ever happened for the patients. When we lose a patient, everybody gets down. But if we're together then we don't dwell on it; we keep going. We keep the patients as strong as possible — minimize the damage."

Chris' motto: "Pump until the pill, take the pill until the cure," refers to the development of an oral chelator that will do what Desferal does without the need for an expensive and complicated delivery device. Such a medicine is under development, Ley says, and effective oral therapy is a matter of time. But a replacement for Desferal — highly specific and almost free of side effects — is not an easy assignment.

Chris' own history with the drug is complicated. Although he was among the first group of patients ever to receive Desferal, he underwent blood transfusions for 18 years before he ever pumped the first drop of chelator. Now, he is one of the oldest thalassemia major patients in the world, and Ley is intensifying his therapy in an attempt to get the accumulated iron out of his system.

Scientists know they can prevent the iron build-up that plagues thalassemics. Ley's question is: "Can we turn them around by aggressively removing it?" Using high-dose chelation — Desferal delivered at three times the normal rate — Ley treats a cadre of four older thalassemics in the Jewish Hospital hematology-oncology outpatient clinic. Over 18 months, the four have gotten no worse, and the levels of iron they are excreting have gone up dramatically. "Can we reverse the consequences of years of iron loading?" Ley asks. "Time will tell."

Chris, who met Ley at a thalassemia conference in Greece, runs his pump 24 hours a day, six days each week. His experience of his disease has created an awareness of his own health and made him a knowledgeable student of medicine. He knows when he needs blood and when he can get by an extra week without a transfusion. At the first sign of a fever, he seeks an emergency room, and he talks to his doctor almost every day.

For others, prospects are not so good. In the third world, all too often finances limit treatment. The cost of administering two units of blood is roughly $500; a year's course of transfusions for a thalassemic therefore approximates $6000. Conventional Desferal treatment costs an equal amount. High-dose chelation might triple that. To add a diabolical twist to the tale, the disease is most common in many parts of the world — India, Southeast Asia, China and the Mediterranean basin — that can least afford to provide care. The somewhat technical reason: thalassemia evolved as a positive adaptation to the malaria that plagues those areas. According to Ley, the parasite responsible for malaria cannot thrive in thalassemic blood cells. So those with the thalassemic trait are resistant to malaria, an advantage in reaching child-bearing age.

In Thailand, one percent of the population has the disease, and Greece's ministry of health, among the world's most enlightened on the subject, spends at least $5,000 per year on each of the identified 4,000 patients in that country. The $20 million total rises by about a million dollars every year.

An oral chelator will help with compliance and may bring costs down, even making treatment feasible for the first time in regions where computer-controlled medicine pumps are as rare as cellular telephones. But it is not the final resolution that Ley is looking for. He seeks a cure, not just a palliation.

That will require corrective measures at the molecular level — an "operation" without a scalpel in a realm just beginning to open up to medical science. The goal is to use highly sophisticated biochemical techniques to keep the genetic switch from ever tripping in those who have defective adult genes for the pro-

Chris Tsangaris' activity is not restricted by either his genetic disease or its treatment.
The computer-controlled and pocket-sized pump delivers chelating medication over a period of time.

Unfortunately, the first drug — the one found by Ley and his colleagues in work done during 1982 to 1984 at the NIH — is still the best. That drug, 5-aza­cytidine, is primarily a chemotherapy agent used in the treatment of leukemia. It reactivates fetal genes (or keeps them active) by changing the chemical environment in which they work. It also "tickles" the bone marrow into making fetal hemoglobin, Ley says. The trouble with 5-azacytidine is that the drug is toxic to cells. It could be tested only on critically ill patients and is not a viable medicine for children who would suffer under its long-term consequences. "It's a howitzer. We have to do it with a bullet," Ley says.

The switch that Ley wants to operate at will "is still a black box." But people who continue to employ fetal hemoglobin into their adulthoods are helping to pry open the lid. Ley's research has revealed that those people also have a mutation in their DNA very near the fetal genes. Ley has discovered that the mutation eliminates a normal DNA structure — a "blip" — near the genes. When the DNA is transcribed, or used as a recipe card, the missing blip may interfere with the ability of a protein to "knock out" expression of the fetal hemoglobin genes.

Put simply, the mutation prevents the switch from being thrown. The blip in the DNA points toward the proteins that work the switch. If Ley can find those proteins that do the switching, then he may be able to suppress them.

Once researchers can do that, they will be able to keep faulty adult genes silent and inoperable. They may also be able to reactivate fetal genes, getting them to make viable fetal hemoglobin. When that vision becomes reality, Chris Tsangaris and his fellow patients will be spared their debilitating health problems and their transfusions, their Desferal pumps and their terrible financial burdens. Chris can look forward to that goal and see progress, even delight in it. But he's not much inclined to think or say "if only." He's not given to dwelling on how his life might have been different. He says instead, "I've already lived longer than I should have. My mother was told I'd never see 14. Three or four times, I've been on my way out. One day I won't be here. That's the reality. In the meantime, if I can do some good and be an example, then I should do it."
A grid imposed on a human heart represents the precision with which medical science approaches sudden cardiac death. Normal rhythm and tachycardia are illustrated, along with normal and disrupted organization of the molecules of the heart's membrane. The circular inset at lower left is a map of an ischemic event: the shaded area represents the region deprived of blood, and the numbers record the ensuing delay in the flow of an electrical wave across the heart muscle.

Research Reveals the Culprits in Sudden Cardiac Death

By Steve Kohler
More than 300,000 Americans — the equivalent of the population of St. Paul, Minnesota or Tampa, Florida — are liable to die sudden cardiac deaths during the next 12 months. Their lives will end unpredictably when their hearts suddenly stop pumping blood.

The problem sounds simple enough — if the heart stops pumping, look to see why. Medical science routinely treats problems that seem to be much more complicated. Upon autopsy, however, the heart muscles of sudden cardiac death victims often appear perfectly normal; no trail is left for medical detectives to follow. And because of the quick and unpredictable nature of the event, only a few cases have ever been recorded as they occurred. Both of those factors, added to the complex nature of what really happens when a heart suddenly stops, have made investigations especially difficult.

But a decade of research by Peter B. Corr, Ph.D., and his colleagues at Washington University School of Medicine has finally revealed the chain of events that occurs in many sudden cardiac deaths. The researchers also have identified the weak link in that chain, the point at which it soon may become possible to interrupt the process and save the life.

"It's an electrical problem," says Corr, who is developing a therapeutic agent that foils the process before it can proceed to its tragic conclusion. The cleverly conceived drug will lie in a potential victim's system until the changes that precede an electrical disruption of the heart's rhythm activate it. Then it will work to forestall the "short circuit" of the heart's electrophysiology and the resulting irregular heartbeat, or arrhythmia, that is the real killer, according to Corr's investigations. It may be a decade before such a drug is available, Corr says.

For the deadly arrhythmia to occur, the change must be abrupt. "If you close off a major supply artery to the heart very slowly, no disruption of the beat will result, because the electrical abnormality in the heart turns out to be relatively uniform. Reopen the vessel slowly, within a narrow time frame, and everything goes back to normal," says Corr. Cells deprived of blood for a long time — 30 minutes or more — usually will die. But if the effect is distributed evenly over the heart muscle, arrhythmias do not occur, Corr explains. "The key to sudden cardiac death as a result of arrhythmia is the heterogeneity (or unevenness) of the effect on the heart," he says.

When the vessel supplying a region of the heart is obstructed and the normal quantity of blood is sharply reduced, scientists say the region becomes ischemic, or deficient in blood. In ischemia, events occur rapidly. Oxygen levels plummet, the biochemical balance of the heart's

Major contributions to various aspects of the work have been made by Jeffrey E. Saffitz, M.D., associate professor of pathology and medicine; Kathryn Yamada, Ph.D., research assistant professor of pathology and medicine; Richard W. Gross, M.D., Ph.D., associate professor of medicine; Burton E. Sobel, M.D., Tobias and Hortense Lewin Professor of Cardiovascular Diseases, and a large contingent of students and post-doctoral fellows.

THE CHAIN OF EVENTS

The most common scenario in sudden cardiac deaths involves the following series of events, says Corr, a professor of medicine and pharmacology.

First, as a sort of trigger, blood supply to the heart is sharply reduced. The presence of coronary artery disease leading to a sudden clot within a vessel is the usual starting point.

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Medical student Kevin Donahue monitoring equipment that produces ischemia, then records the resulting electrical changes in muscle cells in vitro.

Muscle cells, called myocytes, is upset, and the electrical wave that controls the regular pumping action of the heart is disrupted. When the normally smooth flow of that electrical wave is disturbed, the heart's rhythm races as electrical impulses re-enter the loop too soon, triggering extra beats. The condition is called tachycardia.

Finally, in just a few minutes of clock time, the heart can go into fibrillation. Its contractions become chaotic, totally disunified. Corr says the heart then resembles "a bag of worms," all wriggling independently, and no more pumping action occurs. It is this arrhythmia, the result of upset electrical impulses, that is the killer, says Corr.

"The key question," he says, "is 'why does the electrical behavior change so drastically?' What happens to the wave to destroy its uniformity?'" To answer those questions, Corr calls upon the symbol of a wave on the ocean as it encounters a small island. Where the land intrudes on its flow, the wave's regularity is interrupted. The wave breaks, and its pieces encircle the island irregularly, looping back on the main swell and closing on all sides of the land. In an ischemic cardiac event, the electrical wave moving over the delicate membrane of the muscle cells is the equivalent of the sea, and the region deprived of blood is like the island. But there is an added complication: the island moves. "The area of electrical disruption within the ischemic region is not necessarily static; with each beat it can change," adding to the condition's unpredictability and disunity, Corr says.

ORIGINS OF ARRHYTHMIA

That image describes what happens but not why it happens. To understand the mechanisms at work, Corr conducted research on individual myocytes and also on the living hearts of humans and lab animals in which he tracked and mapped electrical impulses as they crossed heart-cell membranes.

Those membranes are made largely of lipid, or fat, molecules. Their highly ordered form is the grid for the electrical impulse that originates at the heart's sinus node, then sweeps across the organ, controlling the beat. An interval in which the heart refills with blood follows before the impulse is regenerated to guide the next beat. When the precise organization of those molecules is disturbed, Corr says, the impulse that travels across them also becomes disordered. Simply put, he has traced the arrhythmia that kills so many to organizational alterations in the heart's membrane.

The heart is a huge user of energy and unusual in its preference for compounds called fatty acids as fuel. Deep in the workings of the individual myocytes, oxidation converts fatty-acid molecules to energy at a tremendous rate, Corr says. So harmful events resulting from the initial ischemic episode occur at a rapid pace.

Two elements called metabolites — players in the complicated oxidation pro-

20
enzymes that normally clear LPC are come from everywhere, he says. But it, disabled. As a result, it's levels rise "two-fold within three minutes of the onset of an ischemic event," Corr says.

LPC is derived from another source: blood cells, the vasculature or the cell membrane itself, Corr is not certain which. The problem in tracing it has been that it is so common it seems to come from everywhere, he says. But it, too, is part of a heart cell's metabolism. Four enzymes normally break it down, but the actions of two of them are blocked by LCA, and a third's activity is reduced as acidity increases.

One of the effects of a reduced oxygen level is acidification. Therefore, as LCA levels increase and the heart becomes more acid, three of the four enzymes that normally clear LPC are disabled. As a result, its levels rise "two-to three-fold within three minutes of the onset of ischemia," says Corr.

When the two metabolites become overabundant, they collect in the carefully ordered structure of the cell membrane, for which they have a chemical affinity, Corr says. Accumulating there, they disturb the membrane's structure, disrupting the integrity of the wave that flows across it and — in short order — inducing an arrhythmia.

Corr has recorded the increased presence of the metabolites in the membranes of individual cells and biopsies from heart tissue, and he has measured the electrical potential across both normal, control cells and their ischemic counterparts, determining that accumulation of the metabolites is largely responsible for the abnormal electrical activity induced by ischemia.

**PREVENTING ARRHYTHMIA**

In untreated animals with blocked arteries that caused ischemic zones in the heart, Corr recorded similar membranous increases in LPC and LCA. However, in animals that had received a new drug — POCA — that works to foil the production of the two arrhythmia-causing metabolites, he found no such increases. By suppressing the enzyme that produces LCA, POCA prevented the accumulation of both metabolites and precluded both tachycardia and fibrillation in all of the animals studied. Corr writes that inhibiting the enzyme offers a "promising approach" for preventing "sudden cardiac death that typically occurs very soon after the onset of acute ischemia in man."

Unfortunately, he says, POCA in its present form is not a viable therapeutic medicine. Because it works to inhibit an enzyme that is prevalent in the body, its effect is too broad. Commenting on the work, Steven Sedlis, M.D., agrees: "POCA's toxic side effects limit its usefulness," he says. Nonetheless, Sedlis, an assistant professor of medicine at New York University School of Medicine, says Corr's research, "has shown that the levels of these two metabolites are higher in ischemic hearts than in controls. In addition, in those ischemic hearts that develop arrhythmias the levels are higher than in those that do not. Even more exciting is his work with drugs that reduce the amount being produced. Such a metabolic inhibitor could make a big dent in the number of sudden cardiac deaths."

Corr is presently developing a drug that avoids POCA's side effects by virtue of its specificity for ischemic tissue. The drug's design puts to work the knowledge that blood-deprived tissue quickly becomes acidic. His goal is to create an enzymatic inhibitor that will be active only in acidic environments. Sedlis calls such a medicine "feasible," and says the concept is "an exciting way of activating the drug only at the site where it is needed."

As physicians become more adept at identifying people at risk for heart attacks and especially sudden cardiac death, they may soon be able to prescribe such a drug as a precaution. Incorporated in the system and silent until it is required, the drug will be activated by the increased acidity associated with an ischemic event. Then, its action of inhibiting the production of LPC and LCA will be invoked, and the two disruptive metabolites will not be overproduced. Despite the ischemia, the regular electrical wave controlling the heartbeat will continue, and tachycardia and fibrillation may be averted.

And, as the only outward sign of all this investigation and intervention, a sizable portion of the terrible number of sudden cardiac deaths will be prevented. In the words of Sedlis, "To me, that sounds revolutionary."
Our Fair Quota: The Nobel Spirit

By Marion Hunt

Herbert Gasser, M.D., left, and Joseph Erlanger, M.D.
At the April 1915 dedication of the Medical School's new buildings Robert Brookings voiced the hope "that we will add, through research activities, our fair quota to the sum of the world's knowledge of medicine." In the 75 years since, three generations of faculty have contributed to that goal. But those who have won Nobel Prizes in physiology and medicine belong in a special category. No other recognition brings with it such glory, and the School of Medicine takes justifiable pride in its Nobel laureates.

Six of the 15 Nobel laureates who have been affiliated with the School of Medicine either were trained here or did their prize-winning work here.

These outstanding scientists served as inspiring teachers to new generations of researchers — transmitting excellence beyond the boundaries of this institution.

In 1944, Philip Shaffer (then Dean of the Medical School) wrote that when Professors Joseph Erlanger and Herbert Gasser became the first faculty members to win the Nobel Prize in physiology and medicine for work done at the Medical School: "the question was repeatedly asked: 'How did St. Louis and Washington University manage it?'"

Answering his own question, Shaffer continued: "We like to believe that the high honors bestowed upon our illustrious colleagues reflect a spirit and a policy that this university has consciously cultivated: a policy to seek for its staff those likely to
see fundamental problems and to be able to divine ways to solve them. The spirit comes when such men and women labor together and thereby stimulate each other.”

Shaffer’s comments proved accurate and prophetic, because only three years later, in 1947, a second Nobel Prize in physiology and medicine came to Washington University Medical School faculty members: Carl Cori and Gerty Cori were notified that they would receive the prize jointly for work on the catalytic metabolism of glycogen. The adverb “jointly” was of special importance; not only had the Coris worked together for 24 years, but they had done so despite opposition to their collaboration. As a woman scientist, Gerty Cori faced particular obstacles.

After finishing medical school in Prague, the Coris had married in 1920 and emigrated two years later. Fortunately, in 1931, Philip Shaffer was wise enough to recruit Carl Cori as head of pharmacology and arrange for a research position and “token salary” for his wife in the same department. (Gerty Cori was promoted to full professor in 1947, the year she won the Nobel Prize.) Far from feeling any resentment at the disparity in their rank, Carl Cori later wrote that this offer seemed remarkable to him: “Then many universi-
ties had rules against employment of two members of the same family.” While their academic rank differed, what counted was continuing their scientific collaboration without added constraints.

Not only did Carl and Gerty Cori work together in brilliant harmony, but they created an intellectual atmosphere that attracted a new generation to science. Among them was Arthur Kornberg who came to work with them in 1947 because, “It was the liveliest enzymology lab in the world, a haven for ambitious, gifted people from all over.” Kornberg joined the faculty in 1953, serving for six years as head of microbiology. He shared the 1959 Nobel Prize in physiology and medicine for his work on DNA replication. Years later, he recalled that in 1947, Gerty Cori drew his attention to Oswald Avery’s paper on DNA, saying simply: “You must read this; it is very important.” Once again, the generous spirit of scientific synergy that Shaffer cited in 1944 led to a new line of research, and another Nobel Prize.

Only 12 years later, yet another graduate of the Cori laboratory (and the Washington University School of Medicine) won the Nobel Prize in physiology and medicine for his discovery of cyclic AMP: Earl Sutherland. A member of the class of 1942, he began to work in the Cori’s laboratory while still a medical student and took a fifth year of study to devote more time to research. He later recalled, “Those early years in the Cori lab gave me the opportunity to work with a number of outstanding investigators. Carl Cori gave me a living example of clear thinking.”

The story of Washington University’s first Nobel laureate indicates that scientific collaboration is indeed the “delicate operation” Carl Cori once called it. Joseph Erlanger and Herbert Gasser mastered the art of making differences complementary rather than adversarial. The senior partner, Erlanger, was “the firm leader of bright people converging on exciting research.” He had been Herbert Gasser’s professor of physiology at the University of Wisconsin; as Gasser later remembered, Erlanger was “such a beautifully clear lecturer...the subject matter he presented amounted to a revelation.” Like his mentor, Herbert Gasser received his M.D. at Johns Hopkins, and in 1916 he joined him in St. Louis.

In 1921, the year Gasser was made head of pharmacology, they presented their first paper using a cathode ray device to record from nerve fibers. The equipment was so sensitive to vibration that their work was done at a concrete bench resting directly on the earthen floor in the South Building’s basement. Their colleague, George Bishop, recalled: “These two men were not particularly sophisticated in either electronics or physics, and their troubles were various and cumulative.” While collaboration demanded painstaking cooperation, differences remained between them because, according to Hallowell Davis, “they did not always share the same interpretation of their own observations.” Nonetheless, they “respected one another’s view, and each held to his own friendly disagreement.”

In 1936, Gasser wrote: “We have long since agreed to disagree as the smoothest way of carrying on this collaboration.” To maintain...
basic differences and mutual respect was no easy task.

Like the Coris, Erlanger and Gasser inspired the work of a new scientific generation — collectively, they were called "axonologists" because they concentrated on neurophysiology. Working in laboratories across the country, their leadership centered at the School of Medicine. In 1944, Helen Tredway Graham described a crucial aspect of their intellectual style. A faculty wife (married to Evarts Graham), she was among Gasser's first appointments in pharmacology. A gifted scientist, she observed her mentor keenly: "To Doctor Gasser, an integral aspect of research is discussion, and in those days discussion seemed never to weary him. Many were the hours spent over endless cups of coffee in the physiology seminar room, in the cafeteria in friends' houses, or in restaurants; and many were the diagrams drawn on odd envelopes, on cafeteria checks, on paper napkins, or even on restaurant tablecloths."

Whether by discussion, instruction, or collaboration, since 1944 the Nobel spirit has continued to flourish here. In 1978, Daniel Nathans, class of 1954, shared the Nobel Prize for "the discovery of restriction enzymes and their application to problems of molecular genetics." Tracing his scientific interests to a summer's work as a second year student with Oliver Lowry in pharmacology, Nathans has said that there he learned "the joy of research" which, he adds, "became a model for my own relationship with students." Thus, the Nobel spirit inspired by outstanding medical-school faculty members is transmitted to a new generation.

Perhaps Carl Cori best described this school's unique quality in analyzing his decision to come here 60 years ago: "Physiology, biochemistry, and pharmacology were housed in one building...it has been claimed that there was something mysterious about this building...it made for success. Actually, it was the spirit of the school, its organization, and its faculty which were largely responsible."
I cannot imagine a more exciting time to enter the medical profession. With the century drawing to a close, we are compelled to look forward into a new era. As the newest generation of physicians, we are charged with setting the goals of our profession and finding solutions to the health-care concerns that currently challenge our society.

Unfortunately, while we face with forging new solutions and systems to meet multiple medical challenges, we must also confront the frustration of implementing change in a conservative profession and an often unresponsive and insensitive government. Indeed, this frustration has led to an unparalleled era of health-care activism by a lay public. Unfortunately, this activism is often poorly controlled and ultimately counter-productive.

In lieu of the educated, considered opinions of health-care professionals, the leading voices of health-care activism are too often those of extremist zealots. While the commitment of these activists is commendable, the inherent contradiction in the violent destruction of research labs by animal rights groups, the bombing of reproductive health clinics and abuse of clinic patrons by anti-abortion activists, and the disruption of a scientific conference by ACT-UP—a group of AIDS activists known for their radical tactics—has discredited the respective voices of these activists.

Although these violent demonstrations effectively focus attention on the issues, the attention is equivalent to our focus on terrorist attacks. These groups do not typically offer constructive solutions to the issues, but when they do, their proposals are discounted as the vehement rantings of crazed radicals. Certainly, we do not want the health-care policies of the future to be dictated by such health-care terrorists.

We need more moderate and considered activism to constructively advance the solutions mandated by the issues. We must remember that attention can be focused by other means. Concerned physicians discussing issues with friends and colleagues, constituents expressing their concerns to legislators, the constructive contributions of ACT-UP developing social programs which support people with AIDS—these all represent effective contributions to altering policies. But certainly, these methods do not galvanize public attention and media coverage to the same extent as more sensational protests.

Peaceful demonstrations and civil disobedience focus public attention with equal intensity as more violent and destructive protests, but without the counterproductive effect. The 1989 March for Women's Lives attracted an estimated 600,000 participants and represented a respected accomplishment for the abortion rights movement. This demonstration was remarkable not only for its size, but for its organization and order as well. Civil disobedience, such as nuclear war protests at the Nevada Nuclear Test Site, focuses public attention without violating the intrinsic integrity of the argument or the participants. The concerns expressed by activists and the solutions they offer are more credible when the forum is non-violent and non-destructive.

We are obligated to get involved. As the newest generation of physicians, we have a vested interest in seeing that the solutions to current and future challenges are medically and ethically viable. To ensure this we must contribute a constructive and educated voice to the activist movements.

With our education comes a social duty to take stands on health-care issues. Clearly, our commitment transcends the immediacy of the physician-patient relationship. We must also contribute as active community leaders addressing the spectrum of health-care concerns. Invest yourself in the future of our profession and get involved by contributing your voice to health-care activism. Discuss the issues with your neighbors and colleagues; lend professional credibility to the arguments that you support. If physicians don't lend a constructive voice to the debate, only the voices of the health-care terrorists will be heard.

Editor's Note

The author, Brad Snyder, M.D., graduated from Washington University School of Medicine in the Spring of 1990. He is currently serving a one-year term as the president of the American Medical Student Association (AMSA), after which he will begin his residency.

The 30,000-member AMSA publishes New Physician magazine, where this column first appeared in the October, 1990 issue (Vol. 37, Number 7). Outlook thanks the publishers for permission to reprint Snyder's thoughtful opinions.
As recently as 20 years ago, ostomy patients were treated with less than fully developed surgical techniques and nagged by social stigmas. Often, they couldn't even get the health-care products they needed from uninterested manufacturers. In St. Louis, that gloomy picture began to brighten when surgeon Sam Schneider "grabbed a surgery resident by the scruff of the neck," took him to a group meeting of ostomy patients and asked, "Why don't you do something to help these people?"

The resident whose neck-scruff was grabbed that evening was Ira J. Kodner, M.D., and the grabbing worked. It provided the seed for what has grown into a regional center for colon and rectal surgery that provides the best possible care, trains nurse specialists, consults with manufacturers of health-care products and educates a surgeon in the colon and rectal specialty each year via what is one of only 25 nationally approved fellowships. Kodner, who today is associate professor of surgery and director of the division of colon and rectal surgery at Jewish Hospital, calls the 20-year evolution "a true example of consumerism. Pressure from patients resulted in better surgical techniques, better training and help from manufacturers."

Perhaps. But the combination of nurturing care and delight in a challenge that characterizes Kodner's nature also has been instrumental. He brought the division out of that germ of an idea and grew it into an active group of three full-time faculty members who investigate cancer, inflammatory bowel disease, and the basic changes in the physiology of the intestine due to aging. The group's large experience treating sphincter injuries establishes its members as experts in the field.

Beyond providing first-rate care to those who need it, Kodner's concern broadens to include work on what he calls "the real quality control of American medicine." He explains: "Every specialty, from family practice to psychiatry, has a certification process that is supervised by two national bodies. Their existence is unknown to the public, and it shouldn't be."

The two components of the quality control team Kodner speaks of are, first, the Residency Review Committee of the American Medical Association that scrutinizes residency programs and certifies those that adequately train specialists. Second comes the system overseen by the American Board of Medical Specialties. Members of each specialty select a board to create and administer an examination that tests for current knowledge and techniques. Only those residents who have completed an approved residency are eligible to take the examination; only those who pass the rigorous assessment of their skills and knowledge become board certified in that specialty.

It is the second arena in which Kodner is particularly active. He says, "All of this is done strictly by volunteers; the 20 boards are composed of physicians who have practices and teaching responsibilities. The general surgery board, for example, requires 38 days each year for six years. Just to maintain adequate standards of care."

Kodner knows that from experience. He sits on that American Board of Surgery,
where he helps to define what constitutes proper training for U.S. surgeons. And he is the recently elected president of the American Board of Colon and Rectal Surgery, a similar board for his own specialty. With characteristic self-deprecation, Kodner says, "After 10 years on the board writing the examination, updating it and administering it, now I'm the president — now I can appoint someone else to do the work."

But clearly he's kidding, because in the next breath he adds, "Washington University has had deep representation on these bodies that make policy for medicine in the United States. I was lucky to be on the general surgery board when Sam Wells (Bixby Professor of Surgery and chairman of the Department of Surgery at Washington University School of Medicine) was its president. And it really is exciting; most other countries do not even have certification programs." Kodner's work leading the board of colon and rectal surgery during the next year will involve creating a recertification program to insure "the maintenance of excellence," as he puts it. Robert Fry, M.D., a partner, a member of the division and a good friend, calls Kodner's contributions to the boards, "outstanding."

Away from the office and the operating suite, Washington University remains an important part of Kodner's life. His undergraduate degree was earned here, and he got his M.D. from the School of Medicine. He served his internship at Jewish Hospital and finished his surgery residency there in 1974. His wife is an alumna of the business school; one daughter is enrolled in the drama program, and a daughter-in-law studies health care administration at Washington University. A second daughter is a student at Ladue High School (with two years to go until she can be considered for admission), and Kodner's son is a medical student at Washington University School of Medicine. "My son did his undergraduate work at Harvard; he's the black sheep of the family," Kodner says.

In concert with the theme of both nurturing and thriving on challenge, Kodner and his family also raise orchids — not a pot here and a pot there, but 500-plus plants of many varieties in a greenhouse attached to the family home. Fry says the greenhouse is "the envy of all his friends. I'm not an orchid person, but this is spectacular."

That interest, established now for 27 years, began as a way to keep alive a family tradition of gardening. Kodner and his wife first cultivated African violets. Though violets are not the easiest plants to grow and test the skills of most horticulturists, for the Kodners the challenge was soon met and interest subsequently waned. When Kodner's wife made him a gift of orchid plants, the new enthusiasm was born.

Why would a surgeon also find lasting excitement in flowers? Kodner has pondered that question and says the two interests may be halves of a single whole. "When you grow orchids, you select perfection; you start with a plant that is already beautiful. The surgeon takes the imperfect and brings it back as close to perfect as he can."

By saying that, he reveals at least one of the forces that compel his life. Whether the subject is flowers, an individual patient's care or the quality controls operating on American medicine, pushing the limits of the possible toward perfection is Kodner's aim.
Joseph Ruwitch Leads Alumni Association

Joseph F. Ruwitch, Jr., M.D. '66, became the new president of the Medical Alumni Association this past July.

He assumes the position from Roger L. Mell, M.D. '65, chief of the division of orthopedic surgery at St. Luke's Hospital.

Ruwitch is an assistant professor of clinical medicine and maintains a private practice of cardiology. He joined the teaching staff of Washington University as an instructor in 1974 and one year later was named as assistant professor of medicine in the cardiovascular division.

Since 1987, he has been a liaison cardiologist in the USA-USSR Exchange in the cardiopulmonary area, under the auspices of the National Heart, Lung, and Blood Institute. He has visited the Soviet Union twice as a guest of the USSR Ministry of Health to meet with Soviet cardiologists involved in epidemiological research similar to that taking place here.

From 1984 to 1989, Ruwitch was a member of the admissions committee for the School of Medicine, also involved in medical school recruitment and helping to redefine admissions goals.

Ruwitch says he is willing to work for the alumni association because he has always felt a "kinship toward Washington University" and because his practice is conveniently within the university environment. As president, he is anxious to see the alumni association continue to expand its current function of providing scholarship support to students. He is particularly interested in increasing the number of endowed scholarships, which are named for recognized faculty members or alumni and funded by the alumni association. There are currently eight scholarships and the association hopes to allocate funding for an additional eight.

During his hours away from the medical school, Ruwitch enjoys trout fishing in Colorado and Yellowstone National Park and recently has taken up golf.

Ruwitch has one son and one daughter, and his wife, Sammy, currently is enrolled in the master's program in early childhood education at Washington University. She teaches at the nursery school on the university's main campus.
Established the Department of Plastic Surgery at Kabul University School of Medicine in Afghanistan from 1967 to 1986. He then went to Kabul, Afghanistan from 1986 to 1989 and established the Department of Plastic Surgery at Kabul University. Theodore Feierabend, M.D. '51, retired in October 1989. From 1952 to 1986 he was a medical missionary to India and was professor of plastic surgery at Christian Medical College in Ludhiana, India from 1967 to 1986. He then went to Kabul, Afghanistan and trained the first two plastic surgeons in that country from 1986 to 1989 and established the Department of Plastic Surgery at Kabul University.

A. Martin Lerner, M.D. '54, recently took office as governor for the Michigan chapter of the American College of Physicians (ACP). As ACP governor, he represents more than 2,000 Michigan internists to the national ACP and oversees membership activities. Lerner is clinical professor of internal medicine at Wayne State University School of Medicine in Detroit. A specialist in infectious diseases, he is in private practice in Birmingham, Michigan.

James E. Darnell, Jr., M.D. '55, has been appointed to the new position of vice president for academic affairs at The Rockefeller University in New York City. As such, he serves as the university's chief academic officer. He has been at The Rockefeller University since 1973, where he investigates the use of viruses to study the mechanisms of gene expression in animal and human cells.

Ruth S. Gurd, M.D. '57, is now emeritus professor of biochemistry at Indiana University School of Medicine. She now resides in Albuquerque, New Mexico.

Lawrence C. Pakula, M.D. '57, recently received the Pediatrician of the Year Award and Leadership Award from the Maryland chapter of the American Academy of Pediatrics. Currently in private practice, Pakula was president of the Maryland chapter from October 1986 until July 1989.

James F. Wittmer, M.D. '57, has been elected as a vice president of ITT Corporation and continues as director of health, environment and safety for that firm. In May, 1990, he was also elected to the board of directors of the American College of Occupational Medicine.

James Jekel, M.D. '60, is the C.E.A. Winslow Professor of Public Health at Yale University and spends his time in teaching and research in epidemiology and public health. He has been married for 32 years, has four children and one grandchild.

John P. Christy, M.D. '63, is currently the president of the Missouri Chapter of the American College of Surgeons. Christy, of Poplar Bluff, will serve a one-year term.

Larry Holder, M.D. '68, practices radiology and nuclear medicine in Baltimore as a partner in a group of 26 diagnostic radiologists. He also serves as chief of radiology at the Children's Hospital and Center for Reconstructive Surgery there and directs the nuclear medicine department at The Union Memorial Hospital. An assistant professor of radiology in the Johns Hopkins School of Medicine, he has recently co-authored a text, Primer of Sectional Anatomy, with MRI and CT Correlation. Married to Washington University alumna Nancy Kauffman Holder (BA '64, MSW '66), he and his wife have three children.

Robert G. Harmon, M.D., M.P.H. '70, is administrator of the Health Resources and Services Administration. Harmon had been director of the Missouri Department of Health since January 1986, as well as clinical professor in the Department of Family and Community Medicine at the University of Missouri/Columbia School of Medicine.

Dennis Cooper, M.D. '71, is one of four Phoenix area physicians honored for his teaching in the premedical program at Arizona State University. He also received the 1990 Teacher of the Year Award from the house staff at Scottsdale Memorial Hospital. Cooper, an ophthalmologist, has been in private practice since 1977.

Charlotte Jacobs, M.D. '72, is the newly appointed senior associate dean of education at Stanford University. This year she was awarded a Presidential Citation from the Head and Neck Society, the Rambar Award for Outstanding Patient Care and the Bloomfield Award for Innovation in Teaching.

Nicholas B. Cooper, M.D. '78, reports that his wife, Elizabeth, gave birth to twins John Lee and Caroline on August 17, 1990.


Robert E. Bechtold, M.D. '79, is associate professor of radiology at the Bowman Gray School of Medicine at Wake Forest University. He joined the Department of Radiology at Bowman Gray as assistant professor in 1984.

W. Grant Stevens, M.D. '80, F.H.S. '86, is the associate medical director of the Marina Breast Center at Daniel Freeman Hospital in Marina del Rey, California. He is a board-certified plastic and reconstructive surgeon.

Brian C. Organ, M.D. '81, is assistant professor of surgery at Emory University School of Medicine. He is married to Stefani Cardwell.

Erika Dale Schuster, M.D. '83, is an obstetrician/gynecologist in Portland, Oregon. She returned to the U.S. in June 1989 after a year traveling in Southeast Asia and the South Pacific.
Thomas Chelimsky, M.D. '83, has been appointed assistant professor of neurology and director of the autonomic laboratory at Case Western Reserve University in Cleveland.

Edward S. Rollins, M.D. '84 and Susan Rollins, M.D. '84 have moved to Johnson City, Tennessee. Edward is a radiologist and Susan is a pathologist.

Gary R. Collin, M.D. '85, is continuing his residency in surgery at Mercy Catholic Medical Center outside of Philadelphia, with planned specialization in trauma.

Nancy Bartlett, M.D. '86, this year began an oncology fellowship at Stanford University.

Justin Starren, M.D. '87, has joined PA Consulting Group at its North American headquarters in Hightstown, New Jersey, where he will work as senior consultant in the company's electronics group. Prior to joining PA Consulting, Starren was affiliated with the department of radiology at Columbia-Presbyterian Hospital in New York, where he directed the design and programming of computerized uro radiology courseware. As part of a joint research venture between Siemens Medical Systems and Mallinckrodt Institute of Radiology, he worked on software that enhances 3-D image processing in cardiac positron emission tomography.

Gladys F. Barker, O.T. '38, is one of ten individuals to receive the OASIS (Older Adult Service and Information System) award presented by the St. Louis Post-Dispatch and KMOX radio. The award recognizes outstanding volunteer contributions to the St. Louis community. Barker's contributions include leading and coordinating groups for OASIS and originating and conducting state sales for the benefit of Miriam School in St. Louis.

Karen S. Flam, O.T. '83, and Terry Kirschner were married April 30, 1989. They live in Boca Raton, Florida. Flam is the assistant director of occupational therapy at Sunrise Rehabilitation Hospital.

Bonnie Helfgott Fisher, H.A.P. '85, has been appointed in-house general counsel for Pitt County Memorial Hospital, Greenville, North Carolina.

John M. Chamberlain, H.A.P. '85, has been appointed medical staff liaison and chief development officer for Glenwood Regional Medical Center in West Monroe, Louisiana.

Marilyn Gruen, H.A.P. '86, and her husband, Douglas Majewski, announce the birth of their son, Daniel Jordan Majewski. They live in Los Angeles, California.

FORMER HOUSE STAFF NOTES

Barbara Stephenson Bruner, F.H.S. '56-'58, retired as professor emeritus from Emory University School of Medicine Department of Pediatrics after 31 years. She was director of the Grady Hospital Pediatric Emergency Clinic and assistant chief of service of pediatrics at Grady when she retired. She will be a consultant pediatrician for both Florida and Georgia Children's Medical Services. Bruner and her husband, John Judson Bruner, have two children.

Robert Maltz, M.D., F.H.S. in medicine, serves on the executive council at the University of Cincinnati College of Medicine, the faculty advisory committee at the University of Cincinnati, and as a member of the board of governors of that institution's alumni association.
Medical scientists may have devised a way to interrupt the chain of events that leads to sudden cardiac death — a chain that includes the tachycardia, or abnormally rapid heartbeat, recorded by this monitor. See page 18.
The holiday season at Washington University Medical Center opened with the St. Louis Children's Hospital Love Light Festival. This year, 2,400 tiny white lights decorate the building and grounds.