Recruits on the Front Lines of Science

The First Biological Sciences Scholars Arrive
Looking back now, the war in Liege was a thrilling experience for us, but thinking of the mangled bodies brought in, it was horrible. Although no one was physically injured in this camp, several showed the strain. The nurses seemed to take it the best… The officers came next, fully admitting their fear, discussing it quite freely, but carrying on from ward to operating room with full efficiency.

—Lt. Col. Harry A. Towsley in the Annual Report of the 298th General Hospital, January, 1945 to June, 1945

Judy Dow Rumelhart’s earliest childhood ideas of Paris do not involve the Eiffel Tower or book stalls along the Seine. What she remembers, thanks to her father’s war stories, are cockroaches. Giant cockroaches. Expanses of cockroaches. “My dad loved describing to us the crunching sound they made as you walked across the barracks floor,” she laughs.

Her father, the late Harry A. Towsley (M.D. 1931, Residency 1934), was a member of the Medical School’s pediatrics faculty from 1934-67 and chair of the Department of Postgraduate Medicine (now known as the Department of Medical Education) from 1967-71. His name is still well known to faculty and staff of the Medical School thanks to the Towsley Center for Continuing Medical Education, which his gift helped make possible, and an endowed fund in his name established with gifts from colleagues and friends to recognize his work.

Towsley, who achieved the rank of lieutenant-colonel in the U.S. Army Medical Corps, was part of the 298th General Hospital unit for more than two years in Europe, and acted as its historian, keeping a diary and shooting thousands of feet of 8-millimeter film. “I remember a long segment that involved cans of Spam,” she laughs. “It was a desperate time, but just as they do on *M*A*S*H*, people made fun of things in order to survive. My father spoke of so much destruction,” she says, “but the thing I most remember is the camaraderie, the deep and very important friendships that evolved for him through those wartime experiences.”

Judy Dow Rumelhart, an Ann Arbor resident, is active in the arts community.
Don Sesqui Wear and Celebrate the Medical School Sesquicentennial!

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Welcome to the third issue of *Medicine at Michigan*.

Last fall was a busy one at the Medical School. The highlight of the season was the October 1 academic convocation held in Hill Auditorium to kick off our sesquicentennial year. The 2,000 guests who attended were able to view our wonderful 15-minute video on the history of the School. Narrated by CBS-TV journalist and U-M graduate Mike Wallace, it celebrates the School’s 150 years of distinction. I opened the ceremony with the following remarks:

“We pay homage today to the legacy entrusted to us, to the scientists, physicians, teachers and researchers, beginning with Regent Zina Pitcher and the first five members of the faculty, Sager, Denton, Douglas, Allen and Gunn, who blazed a path."

“On October 3, 1850, the first medical lecture in the U-M Medical School was presented to 91 students. It was a time before electricity, before natural gas service to Ann Arbor, when Harriet Tubman had just escaped from slavery, Zachary Taylor was the twelfth president of the U.S., and Medical School tuition was five dollars. While we are struck by the contrast in knowledge and technology when compared with today, we find inspiration and challenge in the leadership and vision of the men and women who lived their lives teaching, exploring and healing here in Ann Arbor."

“The Medical School quickly addressed the challenges of its earliest era—cholera and quackery. Ever since, the School’s graduates and faculty have taken part in addressing the medical problems of their era. Early accounts in the *Michigan Alumnus* tell of our graduates’ service in the Civil War. Dean Victor Vaughan was called on to work with Walter Reed to combat typhus during the Spanish American War. The federal government recruited Frederick Novy to study an outbreak of bubonic plague in San Francisco. (The story of those experiments became the inspiration for Sinclair Lewis’s Pulitzer Prize-winning novel, *Arrowsmith.* ) Vaughan also studied influenza following the deadly outbreak at the end of World War I. David Murray Cowie solved the goiter problem by persuading salt manufacturers to include iodine in table salt. In World War II, Michigan men and women again responded to the needs of their time and mobilized to join the 298th General Hospital to care for the wounded in the European theater. Michigan played a crucial role in ending the polio epidemics with the work of Thomas Francis in designing the field trials for Jonas Salk’s vaccine. Our leadership continues with the pioneering work of Francis Collins on the Human Genome Project and Gary Nabel’s recent departure to the NIH to develop a vaccine for AIDS."

“What a fabulous tradition to be part of!

“There are stories, thousands of stories, that could be told of each one of our graduates and faculty by grateful patients, students, and fellow researchers, people whose lives and work have been touched by Michigan doctors. Today we’ve invited some very special people connected with the Medical School to share their personal stories and to be honored on this historic day.”

My welcome was followed by reminiscences and observations on the School and its place in the medical world by a series of distinguished speakers, including Keith Black, a graduate of our School and a neurosurgeon in Los Angeles, representing medical students; David Botstein, chair of Stanford’s Department of Genetics and a former Ph.D. student, representing graduate students; William Hubbard, the tenth dean of the Medical School, representing the School’s administration; Erik Morganroth, who underwent a heart transplant at U-M Hospital, representing the many patients we have cared for; Antonia Novello, former pediatrics resident here and former U.S. surgeon general, representing house officers; and Harold Shapiro, former president of the University, who recounted the fascinating challenges of building the new University Hospital. Gil Omenn, executive vice president for health affairs, and President Lee Bollinger commented on contemporary issues that confront our School and voiced our hopes for the future. Jack Dixon, the Minor J. Coon Professor and chair of the Department of Biological Chemistry, and James Stanley, professor and section chief of Vascular Surgery, did a superb job guiding the ceremony and introducing the speakers. (There are photos of the convocation on pages 44-47 that you should be sure to take time to enjoy.)

The culmination of our year-long celebration of the Medical School Sesquicentennial will take place on October 13-14, 2000, at our annual Alumni Reunion Weekend. I hope to see you this October in Ann Arbor!

Sincerely,

Allen S. Lichter, M.D.
Dean
Yersinia pestis: No Friend to Man

Yersinia pestis, the deadly bacterium that causes bubonic plague, kills by cutting off a cell’s ability to communicate with other immune system cells needed to fight off the bacterial invasion. In a study published in the September 17, 1999, issue of Science, U-M Medical School scientists identify one protein responsible for the plague’s lethal effect and the molecular family it targets.

“In this study, we found that YopJ binds to similar molecules located at the same point in two critical cellular signaling pathways,” Dixon says. The first pathway, called MAPK, controls cell growth and regulates the immune inflammatory response. The second pathway, known as NFkB, also regulates the immune inflammatory response, as well as preventing cell death and controlling embryonic development.

“Scientists thought these two pathways were unrelated, but YopJ recognized a common component in molecules at the mid-point of the MAPK and NFkB pathways,” Orth says. “By binding to this one molecule, called MKK in one pathway and IKKbeta in the other, YopJ cuts the main cellular communications cable and shuts down signaling.”

“Because YopJ is found in many species of bacteria—including salmonella, an intestinal pathogen, and rhizobium, symbiotic bacteria involved in nitrogen fixation—it is particularly intriguing,” Dixon says. “It is rare that a protein effector is found in both plant and animal pathogens.”

“YopJ’s molecular structure is slightly different in other bacterial species and it attacks different types of cells, but all YopJ proteins undoubtedly recognize the same molecules in the signaling pathways,” Dixon says. “This indicates YopJ is an important and effective virulence factor, which has been conserved for long periods of evolutionary history.”

The study was funded by the National Institutes of Health and the Walther Cancer Institute. Collaborators on the study from the Medical School included Zhao Qin Bao, research associate; Scott Stewart, a graduate student; and Amy E. Rudolph, Ph.D., a post-doctoral research fellow. Additional collaborators were James B. Bliska, Ph.D., and graduate student Lance E. Palmer from the State University of New York at Stony Brook.

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Can Aspirin Prevent Antibiotic-Induced Deafness?

Clinical Trials in Xi’an, China, Will Show if Damage Caused by Aminoglycosides Can Be Prevented

Salicylate—the active component of ordinary aspirin—can prevent deafness in guinea pigs exposed to a common class of antibiotics that destroy delicate hair cells in the inner ear. Such are the findings of a study published in the July, 1999, issue of Laboratory Investigation by Jochen Schacht, Ph.D., a biochemist and professor in the Otolaryngology Department, and Suhua Sha, M.D., a research associate in the Kresge Hearing Research Institute at the Medical School.

Clinical trials currently underway at Xijing Hospital, the hospital of the 4th Military Medical University in Xi’an, China, will determine whether aspirin is as effective in people as it is in guinea pigs. The trials at Xijing Hospital are being coordinated by Wei Guo Huang, professor and chair of the Department of Otolaryngology there. “These drugs are a serious problem in rural areas of developing countries, especially China and Southeast Asia, where they are widely used because they are so effective and inexpensive,” Schacht says. “All too frequently, they are the only affordable drugs available. Studies of deaf-mutism in southeastern China showed that two-thirds of the cases were caused by aminoglycosides.”

Discovered in the 1940s, aminoglycosides—which include streptomycin, gentamicin, neomycin and others—are the most widely used antibiotics in the world even though they are known to cause hearing loss and balance disorders in a significant percentage of individuals who take them.

In 1995, Schacht and his colleagues reported their discovery that gentamicin combines with iron in the body to trigger production of free radicals—unstable molecules that rip apart and damage cells. Thousands of tiny hair cells in the inner ear are especially vulnerable.

Other experiments showed that iron chelators—medications used to “soak up” excess iron in the bloodstream—protected guinea pigs from gentamicin’s ototoxic effects. One of the chelators tested was 2,3-dihydroxybenzoate or DHB. In an effort to develop a simple and clinically feasible way to prevent hair cell damage, Schacht and Sha modified the experiment using a related compound called 2-hydroxybenzoate or salicylate.

In subsequent experiments with guinea pigs receiving gentamicin, they were able to show that iron chelators, including salicylate, offer protection against damage to the hair cells of the inner ear.

The research was funded by the National Institute on Deafness & Other Communication Disorders, National Institutes of Health. The experiments were conducted at the Kresge Hearing Research Institute.

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Medical Information Online: The Health of the Data Isn’t Always Robust

Michigan Researcher Sybil Biermann’s Hope: Web Surfers Will Learn the Meaning of “Peer Review”

Patients who search the Internet for advice on treating health problems may be getting information that is inaccurate, inappropriate, misleading or that has not been reviewed by physicians, according to a study by J. Sybil Biermann, M.D., assistant professor of surgery, and her fellow researchers at the Medical School. One of the first of its kind to be published, the study statistically examined a sample of pages retrieved when four Internet search engines sought information on Ewing’s sarcoma, a rare and often fatal form of malignant bone cancer that occurs mostly in children and teen-agers. The uncommon disease was chosen to keep the search results manageable.

Of the 400 pages evaluated in the study, nearly 60 percent had peer-reviewed information from the National Cancer Institute or other reliable sources. The rest contained treatment information that apparently had not been subject to scientific scrutiny.

But, as Biermann and her team wrote in the August, 1999, issue of Cancer in the journal’s lead article, their finding doesn’t mean that Internet users should stop looking for health information—or that doctors should dismiss the data their patients find. Rather, they say, the results should encourage physicians to discuss such information with their patients, and to steer them toward trustworthy sites. “In the meantime,” says Biermann, “the best advice for the public is, ‘Consider the source.’”

Biermann can be reached at biermann@umich.edu.
Soaring above their peers just as their helicopters and airplanes soar above the fields and forests of Michigan and the nation, the U-M Health System’s Survival Flight was named the best air medical program in the country last fall.

The award, given in Nashville, Tennessee, at the annual convention of the Association of Air Medical Services, recognized Survival Flight’s excellence in patient care, leadership, safety, innovation, ingenuity and community service among the more than 250 air ambulance programs in the United States.

U-M’s 16-year-old program makes over 1,300 flights each year, traveling more than 200,000 miles to bring patients and transplant organs to and from the U-M hospitals and other health care facilities. In all, its staff has been involved in the care and transport of nearly 20,000 patients, from critically ill newborns to crash victims and transplant candidates.

Medical Director Mark Lowell acknowledged the Survival Flight team in accepting the award. “All of us at Survival Flight—from pilots, flight nurses and doctors in the air to dispatchers, communications experts, maintenance crews and emergency staff on the ground—take great pride in this recognition,” he said.

“As a surgeon, I treat many patients who have been transported by Survival Flight, and I know how intensely grateful they are for the speed and quality of the team’s service during a critical time in their care,” says Lloyd Jacobs, M.D., professor of surgery and chief operating officer of the University of Michigan Health System. “As an administrator, I am doubly proud to congratulate this fine team on this national recognition of their achievements.”

Strange as it may seem, a form of the vision-threatening disease glaucoma and a rare orthopedic disorder called Nail-Patella Syndrome have a common molecular history. A research effort headed by scientists at the University of Michigan Department of Ophthalmology and Visual Sciences has shown that these two vastly different disease manifestations are the shared effect of a mutation in a single gene.

Increased pressure in the eye, damage to the optic nerve, and a decrease in the field of vision characterize glaucoma, one of the most common causes of visual loss. When left untreated, glaucoma will rob a person of sight. The National Eye Institute estimates that three million Americans have glaucoma, and that of these, 120,000 are blind. Half the people in whom the disease process has begun do not realize they have glaucoma until irreversible damage has occurred. More than a dozen glaucoma genes have been mapped or cloned so far.

Nail-Patella Syndrome, on the other hand, is rare. Its incidence is one in 50,000 births, and its name derives from two of its most evident characteristics, absent or ridged nails of the hands and absent or small knee-caps (patellae). A variety of other orthopedic features of the disease can affect mobility, and surgery is required in some cases. NPS has long been accepted as a familial disease, and one of the first genetic linkages discovered in humans in the 1950s placed the NPS locus near the ABO blood group genes on chromosome 9. The characteristics of NPS have been reported in the orthopedic literature for more than 100 years, but
throughout its long history no one had figured out that glaucoma can be one of the characteristics of the disease.

Physicians and researchers in the Department of Ophthalmology and Visual Sciences discovered the curious association between these two disparate conditions. Paul R. Lichter, M.D., F. Bruce Fralick Professor and chair of the Department of Ophthalmology and Visual Sciences, is a glaucoma specialist who collaborates with basic scientist Julia E. Richards, Ph.D., a molecular geneticist and senior research assistant, in a study of genetic defects underlying the hereditary forms of glaucoma. Together, Richards and Lichter have been tracking the clinical characteristics of glaucoma as part of their study of the relationship between phenotypes and genotypes.

In a classic example of what can be accomplished by a perceptive clinician, Lichter noticed that one of his glaucoma patients had no thumbnails. Lichter remembered that when he had treated this woman’s mother for glaucoma, he had observed a similar lack of thumbnails. “Dr. Lichter made a connection between NPS and glaucoma that had not been made by a century of physicians studying this syndrome.”

 had not been made by a century of physicians studying this syndrome. And it’s easy to see why it would have been missed. When a child with NPS goes in to have surgery, the orthopedist has no reason to ask if grandmother uses eye drops,” says Richards. Further investigation showed that six family members had glaucoma plus NPS, and that a similar association between the two diseases was present in a second family.

Lichter and Richards teamed up with Michael Boehnke, Ph.D., in the Medical School’s Department of Biostatistics to evaluate the relationship between NPS and glaucoma. Linkage analysis provided strong evidence of a genetic relationship between NPS and glaucoma, and showed that NPS in these families was linked to the known NPS locus on chromosome 9. To answer additional questions, however, identification of the actual NPS gene was needed. Collaboration with Iain McIntosh, Ph.D., at Johns Hopkins University resulted in isolation of a “contig,” an overlapping set of clones spanning the region of chromosome 9 that contained the NPS gene.

Another collaboration, this time with Douglas Vollrath, M.D., Ph.D., at Stanford University led to the determination that the NPS gene is the human transcription factor gene LMX1B. “Dr. Vollrath called us to suggest LMX1B as a candidate NPS gene based on its location and its functional characteristics,” says Richards. “When tests showed it was present at the right location in the contig of clones, we were off and running to clone and sequence the gene and test for mutations in the patients. It was a very exciting time and everything happened rather quickly after that.”

Since then, the Michigan-Stanford collaboration has found mutations in a dozen NPS families and has shown that the glaucoma and orthopedic characteristics present in a given family are likely both the result of the same mutation in LMX1B. Many questions remain to be answered about the level of glaucoma risk faced by someone affected by NPS, since there are NPS families in which glaucoma is not found. However, it is clear that glaucoma is not a rare finding among older individuals with the syndrome, and people with NPS should be made aware of their risk of glaucoma. A recent paper co-authored with U-M orthopedist Frances Farley, M.D., has alerted the orthopedics community to the importance of referring NPS patients for glaucoma screening.

This kind of collaboration between basic scientists and clinicians can identify underlying genetic defects and pave the way to a better understanding of diseases. In this case it revealed a relationship between the orthopedic and ocular characteristics of NPS.

Lichter can be contacted at plichter@umich.edu, Richards at richj@umich.edu.


The University of Michigan Hospitals have moved back onto the “Top 10” list of best hospitals in America, according to the 1999 survey released by U.S. News and World Report magazine. The U-M Hospitals ranked ninth, up from a ranking of 12th in 1998.

Thirteen hospitals in America made this year’s every category and showed improvement in several areas.

The U-M received recognition in 14 of 16 specialties considered, with six specialties ranked ninth or higher and 12 listed in the top 20 in their respective categories. Specialties making the biggest gains were cancer, which jumped to the number nine spot nationally after being ranked 20th in 1998, and orthopedics, which ranked 14th after coming in at 36th in 1998.

Overall, 1,881 of the nation’s 6,299 hospitals met the magazine’s eligibility requirements. The final rankings encompass 188 different hospitals. The concept and design of the statistical model used for the rankings were created by the National Opinion Research Center at the University of Chicago but have a distinct Michigan connection. They are based on a theme called the Donabedian paradigm, created by Avedis Donabedian, professor emeritus, health management and policy, in the U-M School of Public Health.
Viral Tethers: A Concept to Explain the Long and Often Hidden Life of Latent Viruses

U-M cancer researchers Erle Robertson, Ph.D., associate professor of microbiology and immunology, and graduate student Murray Cotter have authored the first study to identify a specific tethering mechanism between a virus and its host cell. Their findings were published in the November 25, 1999, issue of Virology.

Robertson and Cotter have discovered how some viruses can hide inside the nucleus of human cells for long periods of time—without producing symptoms or triggering an immune response—by attaching to host cell chromosomes. The viruses survive by going dormant until a weakened immune system allows infected cells to begin multiplying wildly.

Robertson and Cotter describe a series of experiments with Kaposi’s sarcoma-associated herpesvirus or KSHV—a human virus associated with the type of cancer called Kaposi’s sarcoma. In their studies, Robertson and Cotter found a protein expressed by one gene on the virus that builds a biochemical docking station that links viral DNA to the chromosomes of lymphoma cells.

KSHV is one of a family of gammaherpesviruses known to remain dormant in humans long after the initial infection is over. Other similar viruses include the Epstein-Barr virus; the human papilloma virus, which causes cervical cancer; and viruses responsible for hepatitis B and hepatitis C.

“We’ve always suspected that latent viral DNA couldn’t survive long-term within cells without some type of tethering,” says Robertson. “But the latency mechanism for these viruses has been a black box. Now we have a key that will get us in the front door.”

Using cultures of lymphoma cells infected with KSHV, Robertson and Cotter identified a protein called the latency-associated nuclear antigen or LANA, which is expressed by one of approximately 80 genes encoded by the virus. They found that LANA binds to three regions of the KSHV genome, but is most likely to lock onto one specific region for tethering the virus to host chromosomes.

In addition to viral DNA, the U-M scientists found that LANA also binds to histones—small proteins that link bundles of DNA called nucleosomes to make chromatin fibers, which are folded and packed to form chromosomes.

“The results suggest a biochemical mechanism that binds elements of viral DNA to host chromosomes through the interaction of LANA, histone H1, and possibly other chromosomal proteins,” Robertson says.

Robertson has evidence of a similar tethering mechanism in the Epstein-Barr virus, which infects immune system cells called B-lymphocytes. Associated with several varieties of cancer, including breast cancer, Epstein-Barr virus is found in more than 90 percent of the world’s population. In most people, a healthy immune system keeps the virus suppressed. If something upsets the balance between virus and immune response, however, the virus can re-activate. The trigger that signals a dormant virus to begin multiplying and infecting new cells remains unknown, according to Robertson.

“This tethering mechanism may give us clues that we could use to develop more effective gene therapy vectors.”

In previous studies with Epstein-Barr virus, scientists identified a protein called EBNA1, which binds to B-lymphocyte chromosomes. Since EBNA1 is expressed in all EBV-infected cells and LANA is expressed in all KSHV-infected cells, Robertson believes they may have similar functions. “We haven’t linked all the pieces yet, but it is extremely likely that EBNA1 is part of a similar tethering mechanism for Epstein-Barr viral DNA,” he says. “If there are two viruses with the same mechanism, then there probably are more.”

HIV, the virus that causes AIDS, is a different type of virus and is unrelated to the U-M study, Robertson notes. However, Kaposi’s sarcoma is a common cancer in people whose immune system has been suppressed by the AIDS virus.

In future research, Robertson and Cotter will try to find LANA’s exact binding site on Kaposi’s viral DNA and on histone proteins. “Once we understand the biochemistry of the tethering site, we can start developing therapeutic agents to block it. Blocking the binding site could mean the difference between just treating symptoms and eradicating these viruses from the host population,” adds Cotter, a Medical Scientist Training Program (M.D./Ph.D.) student in cellular and molecular biology.

Cotter also hopes to apply what he learns from KSHV biology to gene therapy research. “The central question in gene therapy is how do you stabilize foreign genes in a cell’s nucleus, so they will express beneficial proteins over long periods of time,” he says. “This tethering mechanism may give us clues that we could use to develop more effective gene therapy vectors.”

The U-M has applied for a patent on the viral tethering mechanism. The research was supported by the National Cancer Institute, the American Heart Association, the Leukemia Society of America, and the Health System’s Comprehensive Cancer Center.

Robertson can be reached at esrobert@umich.edu; Cotter can be reached at macotter@umich.edu.
Peripheral arterial disease affects more than six million Americans. Although not fatal in itself, individuals with it may die of complications of coronary artery disease and, less often, of complications of cerebrovascular disease. Now, researchers at the Medical School are studying a new growth protein that shows promise in stimulating the body to grow new blood vessels. They hope to determine if the protein, called recombinant fibroblast growth factor-2 (rFGF-2), can help increase blood flow to the legs by encouraging the growth of collateral arteries around the blockage—in essence, stimulating the growth of natural by-passes.

Investigators in the Therapeutic Angiogenesis Program hope to determine if rFGF-2 and similar proteins that promote new blood vessel growth can provide a non-surgical alternative for those with peripheral artery disease. The study is called TRAFFIC (Therapeutic Angiogenesis of rFGF-2 for Intermittent Claudication), and the Medical School is one of two institutions coordinating the trial, which will be conducted at 20 U.S. medical centers.

RFGF-2 is a genetically engineered form of a protein produced naturally in humans that stimulates the growth of new blood vessels. The protein has shown promise in recent studies at the U-M as a potential treatment for angina in patients with coronary artery disease. Previous investigations of rFGF-2 showed that it stimulated the growth of new blood vessels in animals, and earlier clinical studies showed that it was well tolerated by humans across a wide range of doses.

“This study is the largest one to date examining therapeutic angiogenesis as a therapy for peripheral artery disease,” says Robert J. Lederman, M.D., an interventional cardiologist and assistant professor of internal medicine. Lederman serves as the national co-principal investigator on the study. “Therapeutic angiogenesis is very exciting because there is great potential to improve severe and debilitating symptoms in patients who are not eligible for conventional surgical or catheter-based treatments.”

Researchers elected to conduct the study in Israel because three different ethnic populations there have very different risks of colon cancer. Individuals of Ashkenazi Jewish descent have relatively high rates of colon cancer, whereas colon cancer is rare in people of Arabic descent. Sephardic Jews have an intermediate risk of colon cancer.

“It is not clear why different populations within Israel have such different risks of colon cancer, nor do we understand the influences of immigration,” says Gadi Rennert, M.D., Ph.D., principal investigator of the study and assistant professor of internal medicine and epidemiology.

More information about the Michigan Therapeutic Angiogenesis Program is available on the Web at: http://www.med.umich.edu/tap/.

Lederman can be contacted at rlederma@umich.edu.
Using Mathematics to Understand a Species of Bacteria That Can Add Up to Big Trouble:

*Helicobacter pylori* is Sometimes Hard to Stomach

About half of all adult Americans have an intimate companion—one they carry with them everywhere—that usually keeps its presence unknown but can prove to be a most unwelcome guest. Its proper name is *Helicobacter pylori*—a species of bacteria which usually produces no symptoms in the humans carrying it, but which can cause ulcers and stomach cancer in some individuals.

Though it is an organism widespread in the human population, scientists know very little about *H. pylori*. To learn how it coexists for long periods of time with people, Medical School scientist Denise Kirschner, Ph.D., created a mathematical model, based on experimental evidence, of the symbiotic relationship between bacterium and host. Results from the model were published in an article by Kirschner and Martin Blaser, M.D., of Vanderbilt University Medical Center in the July 20, 1999, issue of the *Proceedings of the National Academy of Sciences*.

While several mathematical models have been developed to study HIV, the virus that causes AIDS, this is the first model for *Helicobacter pylori*, according to Kirschner. “The most important factor in the relationship is the capacity of the host response to the bacteria,” says Kirschner, an assistant professor of microbiology and immunology in the Medical School. “Some people have the ability to flush *Helicobacter pylori* from their systems and some don’t. We don’t know why these individual differences exist and we don’t understand exactly how the host responds to the bacteria’s presence. The response may or may not be directly related to the immune system.”

“Some people have the ability to flush *Helicobacter pylori* from their systems and some don’t. We don’t know why these individual differences exist and we don’t understand exactly how the host responds to the bacteria’s presence.”

“Everything about the model works and is consistent with indirect experimental data,” Blaser says. “We describe the initial transition from one organism to a bloom of organisms. Then as immunity kicks in, the organisms settle down and reach equilibrium. In essence, bacteria and host are dancing together; each one is signaling the other.”

*Helicobacter pylori* bacteria live in the thick mucus layer lining the inside of the stomach, which protects epithelial cells from stomach acid, Kirschner explained. When bacteria enter the stomach, probably through fecal-oral transmission, some penetrate the mucus layer and attach to epithelial cells. These bacteria release molecules that irritate and degrade epithelial cells, which creates food for the bacterial colony.

“Our most surprising discovery is the key role played by this small group of adherent bacteria,” Kirschner said. “They only make up one percent of the entire colony, but they must be present or colonization will not take place.” The model also indicates that two competing strains of *H. pylori* can live together in the stomach at the same time—but not for long. “One strain will always be dominant over the other,” Kirschner says. “But any change in stomach conditions can create advantages for a different strain and allow it to predominate.”

“Mathematical models like this one are especially valuable in biomedical research when clinical experiments are difficult or impossible,” Kirschner says. “They help us focus study on areas most likely to produce a positive result and allow us to test experimental treatments quickly and inexpensively to guide human clinical trials.”

Model development was supported by the National Institutes of Health, the Medical Research Service of the Department of Veterans Affairs, and Astra-Merck, Inc.

Kirschner can be reached at kirschne@umich.edu.
James Woolliscroft Named Executive Associate Dean

James O. Woolliscroft, M.D., professor of internal medicine, the Josiah Macy, Jr. Professor of Medical Education, and associate dean for graduate medical education, has been appointed executive associate dean of the Medical School.

"Jim’s expertise and vision have been invaluable to me during my first year as dean, and I look forward to his help as we continue to position the University of Michigan Medical School to be the best in the country," said Dean Allen Lichter upon Woolliscroft’s appointment. “We are thrilled to have Jim increase his role in Medical School administration.”

Woolliscroft’s responsibilities as executive associate dean include assisting in the management of day-to-day operations of the Medical School. He has direct responsibility for working with the associate deans for clinical affairs, student programs, medical education, faculty affairs, and research and graduate studies. "Jim will be integral to the School’s strategic planning and priority setting and the development and implementation of new initiatives," said Lichter. Woolliscroft continues to oversee graduate medical education and the new school-based initiatives in telemedicine, tele-education and international health.

Woolliscroft received his M.D. degree from the University of Minnesota in 1976. He completed his internship and residency training in internal medicine at the University of Michigan in 1980. He was appointed to the U-M Medical School faculty in 1980 as an instructor in the Department of Internal Medicine, and achieved the rank of professor in 1993. Woolliscroft was selected as the nation’s first Josiah Macy, Jr. Professor of Medical Education, an endowed professorship awarded by the 70-year-old New York-based Josiah Macy, Jr. Foundation, in 1996. Since the mid-1960s the Foundation has focused on the education of health professionals, particularly physicians.

In addition to his clinical activities as a general internist, Woolliscroft is a nationally prominent researcher and has published extensively in the field of medical education. Throughout his academic career at Michigan, Woolliscroft has been an institutional leader in the application of educational theory to physician education. He served as course director for clinical skills, introduction to clinical sciences, and the internal medicine clerkship.

He served on the Dean’s Committee on Curriculum Improvement, the committee that laid the groundwork for the revision of the Medical School’s curriculum. He was associate chair of undergraduate education in the Department of Internal Medicine from 1987-1994. In 1995 he was elected to a two-year tenure as chief of clinical affairs of the University of Michigan Hospitals. In conjunction with his role as chief of clinical affairs, he also served as assistant dean for clinical affairs in the U-M Medical School. In 1998 he was appointed associate dean and director of graduate medical education.

Pediatrician Betsy Lozoff Becomes Seventh Researcher in Medical School to Win Special MERIT Award from NIH

Her Award Will Allow for Further Research on Iron Deficiency

Betsy Lozoff, M.D., director of the U-M Center for Human Growth and Development, has received a National Institutes of Health MERIT (Method to Extend Research in Time) Award for her work on the long-term behavioral, developmental, and physical effects of iron deficiency—the world’s most common single nutrient deficiency.

Iron deficiency anemia affects roughly 25 percent of the world’s babies, and iron deficiency without anemia affects many more. In 1981, Lozoff, who is also a professor of pediatrics and communicable diseases in the Medical School, began studying a group of 191 Costa Rican babies with iron deficiency and has conducted follow-up studies when the children were 5 years old, 10 to 15 years old, and 15 to 16 years old.

Even though their current health status is excellent, she has found that adolescents who were iron deficient as infants have lower achievement test scores in reading, writing and arithmetic, and more behavior problems, especially related to anxiety and depression.

The new grant will allow Lozoff and her research team to assess cognitive, motor, and emotional functioning at age 19. The goal is to learn how early iron deficiency affects a wide range of behavioral, developmental, and physical characteristics of young adulthood, including the pursuit of higher education, job stability and level, mental health, early childbearing, obesity, stunted growth, and cardiovascular health.

The highly selective MERIT awards, provided to fewer than five percent of NIH investigators, go to researchers who have demonstrated superior competence and outstanding productivity during their previous research endeavors. The awards provide the opportunity to gain up to 10 years of support. Lozoff is one of just a handful of MERIT recipients at the U-M.

Lozoff can be reached at blozoff@umich.edu.
Wanting to Know What No One Has Ever Known Before: Six Young Stars Chase Their Dreams at Michigan

By James Tobin

The surfaces in Sean Morrison’s brand-new office in the Cancer Center are utterly clean and bare. In the nearby labs of Zhaohui Xu and Tom Wilson and Brian Akerley in the Medical School, research benches and storage shelves are only beginning to accumulate their loads of beakers and flasks. Even the quarters of Kathleen Collins and John Moran, who arrived at Michigan a year ago, harbor little of the clutter that grows only from long labor in one spot. Each of these six places says: “Something is starting here. This is the beginning.”

Together, these six beginnings make up a milestone. Collins, Moran, Xu, Akerley, Wilson and Morrison are the first University of Michigan Biological Sciences Scholars — the fruit of an annual commitment of up to $2.5 million by Gilbert Omenn, CEO of the Health System and the University’s executive vice president for medical affairs, to recruit, in his words, “the equivalent of the ‘best athletes in the draft,’ the most promising faculty candidates from top labs at top institutions.”

The appointments of these six are in the Medical School; future “classes” of Biological Sciences Scholars may include appointments in departments outside the school as well. They are among the first recruits to the University’s emerging Life Sciences Initiative, an intense, long-term effort to lead the world in the momentous advances in biological understanding that are only beginning with the nation’s Human Genome Project, directed by U-M Medical School geneticist Francis Collins. No one knows, of course, which scientists in which nations will do the work that makes 21st-century scientific history. But the interdisciplinary research committee who chose these young scholars believes they stand as good a chance as any. (The committee is currently headed by Michael Marletta, Ph.D., professor of biological chemistry in the Medical School and the John Gideon Searle Professor of Medicinal Chemistry in the College of Pharmacy).

While these sparsely furnished workspaces may be portals to the future, they also represent six culminations. They are the prizes at the end of six long paths of persistence and inspiration and perhaps especially of a rare form of devotion — and of joy. In academic training, no trail is longer than that of the medical scientist, and without a “joyful sense of superior intellectual power,” as Albert Einstein once described the pleasure of being a scientist, they might not have come this far.

They share with all young biological scientists of the day a special luck of timing: that of coming to the world of medical science when it is poised on the brink of fabulous new discoveries. University of Michigan President Lee C. Bollinger, who is determined to change the landscape of the life sciences at Michigan in the coming years, has compared the postgenomic world of the biological sciences to the ferment in physics in the early decades of the 1900s, the flurry of intellect focused on constitutional law, his area of study, in the 1960s.

But their stories also encompass the inspiration and triumph that have been a part of science forever: the college student who almost became a millionaire but kept right on going when he didn’t; the 10-year-old who decided to become a scientist when he overheard the groans of the dying woman who had taken care of him for many years of his childhood; the experiencing by a beginning scientist of an unexpected “eureka” moment in the quiet of a late December eve, with the accompanying certitude that an entirely new idea had just found its way to formulation in her head.
In the late 1960s, John Moran’s family moved from their blue-collar Queens neighborhood of Jackson Heights out to the more suburban Holtsville, Long Island, 45 minutes east of the city. But his dad still did the work he’d always done — commuting back to the city every day to supervise crews fixing Manhattan’s underground phone lines.

That was the prototypical career path among Moran’s childhood friends—toward the practical jobs that keep the world running. “We didn’t use a lot of big words,” he says. “Not many people said ‘extemporaneously’ where I grew up.” Up to high school, he and his younger brother either studied or played sports in the street. It was one or the other, their father said. When the boys turned 16, he gave them a choice — find a job on their own or go to work in the sewers. So the teen-ager spent his summers ripping out and refitting the insides of old buildings.

But his dad also saw his older son’s remarkable grades in science and math, and he made it clear that Moran was headed for college. He chose the Rochester Institute of Technology, sight unseen, because it offered him the most scholarship money. Except for a senior trip to Washington, D.C., he’d never left metropolitan New York in his life. He packed his car while his dad reminded him: “You’re not going there to party.”

Rochester’s commitment to preparing students for technical careers might be called ferocious. In four years Moran was allowed four electives. Students at Rochester take classes for a term, then work for a term, so he found a job at a pharmaceutical plant, mixing anti-fungal compounds for medicinal chemists. In class he had to compensate fast for a shortage of high school lab experience. In one early outing he mistakenly set the room on fire. ➤
In organic chemistry, he and a friend got into a pattern with a professor named Kay Turner. She would hand back a test, point to one of their solutions, and say, “This is right, but my way’s quicker.” Moran and his friend would look it over, produce a faster route to the answer, then hand it back. Turner would glance at it again and say, “Your way’s quicker, but my way gives a higher-percent yield.” To Moran, it was just fun. Then one day Turner said, “You know, you guys think this is a game. But not everyone can do this.” “That’s when I started to realize, ‘Wow, maybe I got a knack for this stuff,’” Moran recalls.

He had chosen to major in medical technology by flipping through the Rochester catalog and pointing a finger. When another professor invited him to switch to biochemistry, Moran discovered an infinitesimal realm of cause and effect that appealed to him immensely. “At the molecular level, biochemistry was telling you how things work,” he says. “You were going into the nitty-gritty. Plus, it was just generally cool. It floated my boat. It was concrete. There were answers.”

When Kay Turner told him there was a good Ph.D. program in biochemistry at Ohio State University, he applied and was accepted. When somebody called to tell him some paperwork was needed, he got in his car, drove all night to Columbus, slept in the car outside Ohio Stadium, woke up, walked into an office, filled out the papers, got back in the car and drove home to Rochester. “I wasn’t a big guy on, like, planning out where I go in life,” he laughs. “I was just kinda like, okay, I get in the car and I go there.”

He arrived in Columbus in the fall of 1986. A few months earlier he had met the woman who would become his wife — Robin Sullivan, an electrical engineering student at Rochester. Now he fell in love again, with genetics.

“It made sense,” he says. “It was really, purely logical. When you looked at genetics, it was like — the traceability of it — wow, that’s cool. The problem-solving was cool — how you could play with DNA, cut DNA, sequence DNA, do recombinant DNA work. You could get a handle on what actually was occurring.”

At long last, Moran was becoming aware that his grasp of science was not like everyone else’s. When his mentor at OSU, Philip Perlman, suggested that Moran follow him to the rarefied environment of the University of Texas Southwestern Medical Center at Dallas, home to three Nobel laureates, Moran got back in his car. In Dallas he studied mobile introns in yeast mitochondrial DNA — that is, pieces of DNA that move from one place to another in the yeast’s genetic sequence. He took his Ph.D. in 1994. For his postdoctoral work, he set his sights on the mysteriously shifting pieces of human DNA called Long Interspersed Nuclear Elements, or LINES — distant descendants in the human genome of the introns he had studied in yeast.

LINES are often classified among the genetic elements called “junk DNA” because they seem to have no clear function. Yet scientists are intrigued by their ability to leap from one place in a genetic sequence to another, sometimes dragging adjacent genetic elements along with them. These movements are thought to hold promise for understanding and possibly for treating a host of inherited diseases, including cancer.

So in the spring of 1994, Moran was back in his car — first to Baltimore, where Haig Kazazian ran a leading LINES laboratory at Johns Hopkins University, then to the University of Pennsylvania when Kazazian moved his lab there. Understanding LINES became Moran’s obsession — why some leap and some don’t, how they move and how often, and what these characteristics might imply for medicine. While he acknowledges that the mapping of the human genome is a revolutionary step, he notes that a map, after all, is only a tool for exploration. “The thing that people are still gonna need to figure out is how things work,” he says. “There’s not gonna be a simple solve to the how-things-work problem. There’ll be inferences, but until you get down in the trenches and figure it out, you won’t know how it works.”

Moran, who looks and sounds like an affable ex-Marine, fills his speech with its own kind of junk DNA — a lot of New York-inflected “and-stuff-like-thats” and “Hey, whatevuh.” But when the conversation moves deep into his work, the street riffs give way to precise blends of scientific sophistication and pithy simile, as when he likens genetic strands to Lego blocks, the tiny plastic children’s blocks that can be shaped into structures of infinite variety. All of a sudden, the thick-necked guy who says things like “I didn’t walk around and start sitting there and expousing like I knew something” is saying: “Our hope is that a true understanding of the biochemical and molecular mechanisms by which these elements move will ultimately help us better understand human disease processes.”

Clearly, the professors who recruited Moran to U-M’s Departments of Human Genetics and Internal Medicine were charmed by the combination. “John’s enthusiasm for, and excitement about, his research — and about science in general — were impressive and infectious,” says Thomas Gelehrter, M.D., chair of the Department of Human Genetics. “The clarity with which he was able to describe complicated genetic experiments reflected the clarity and incisiveness of his scientific thinking.”

Moran shrugs. “Once I start talking about science, I get excited, you know? I get pumped. I like the stuff. I work at my hobby.” As for his back-door path to a position that any product of Caltech or Yale might envy, he says, “Look at Kurt Warner for the Rams right now. The guy played arena football for the Iowa Barnstormers and now he’s, like, the most prolific passer in the game. If you keep doing it, you don’t have to be at the elite schools, coming up. If you’re into it and you love what you do, you’ll get there.”
It seems to violate some unspoken protocol for scientists to talk about the competitive nature of what they do. Overt discussion of competition is for athletes and entrepreneurs. Which, no doubt, is why talk of competition in science comes more easily for Sean Morrison, who has been all three — scientist, athlete and entrepreneur.

Entrepreneur came first.

Growing up outside Halifax, Nova Scotia, Morrison was a hands-on science guy from an early date. “The older I got, the more excruciating it was to sit there and listen to people talk about science rather than doing it,” he says. In his science fair project in his senior year of high school, he and a friend studied *mycorrhizae*, a fungus used in agriculture to increase nutrient uptake in plants — an earth-friendly fertilizer, but expensive to grow. When they found a better way to grow it — hydroponically (in water) — a profit-making enterprise was born. Dalhousie University, which had already recruited the two as students, lent them a lab. The Canadian government gave them a grant. They hired staff. When his partner dropped out of the company to focus on his classes, Morrison quit school to work on the company full-time.

He spent a quarter-million dollars on research. He needed $3 million to bring the fungus to market. By the time he was 20, he had talked to every significant investor in agricultural biotech in North America. But it was the late 1980s. The American stock market had just crashed, and no one was investing in agricultural biotech. Morrison closed the door on Endogro Systems, Inc., packed two years of college courses into 12 months, and sent off his applications to major graduate programs in immunology. “I wanted to get into medical research,” he says, “because medical research is more competitive than agricultural research. I wanted to spend time on things that people considered important problems, and where, if you were successful in solving a problem, it would be something that people felt really mattered. And I really enjoyed the competition.”

He chose Stanford over Harvard and Oxford, not just for the California weather but to work in the lab of Irving Weissman, who was doing pioneering work with hematopoietic stem...
Sean Morrison continued

cells, the rare cells in bone marrow that generate all the other cells in the blood and immune systems. By the time he finished, he was considered one of the most promising students in his field in the world. But he wasn’t the type to spend every night in the lab. After all, the Stanford club hockey team played every Tuesday, Thursday, Friday and Saturday night, not to mention road trips, and Morrison was its regular right wing. “I wasn’t good enough to play varsity hockey in Canada, but I was good enough to play in California,” he says. He married halfway through his fourth season and hung up his skates when his first child arrived. “It was forced retirement, and it’s still painful,” he says with a wry smile, “but it was time to move on.”

Next came post-doctoral work in David Anderson’s lab at Caltech, where Morrison used techniques he had learned in Weissman’s lab to isolate the stem cells that give rise to the peripheral nervous system. That set up the work he is now preparing to do at Michigan, where he will investigate whether stem cells from various types of tissues use the same set of genes to replace themselves. If that’s the case, the implications may be profound. If, for example, all kinds of stem cells use a common genetic program to make more of themselves, it’s possible that a misfiring of that program is related to the deadly proliferation of cancer cells. Identifying the genes involved in that malfunction could produce new targets for genetic treatments in cancer. His work is stirring real excitement among his new colleagues in the Department of Internal Medicine’s Division of Molecular Medicine and Genetics. “He is without a doubt one of the brightest, most innovative researchers I have ever met,” says Michael Clarke, M.D., professor of internal medicine, who worked with Morrison for a time at Stanford. David Ginsburg, M.D., Warner-Lambert/Parke-Davis Professor of Medicine and chief of the division, calls Morrison simply “a superstar.”

Describing what drives him, Morrison reaches for an analogy to his second-favorite sport. “Science is like golf,” he says. “It’s not like hockey or football. In hockey and football, you want to go out on the field and destroy your opponent and beat him physically as well as on the scoreboard. In golf, you’re basically playing against yourself, and no matter how well you do, there’s always room for improvement. I don’t sit in my laboratory and I don’t stand on the golf course trying to beat so-and-so. I just am trying to do better and better, to improve the quality of the science I do and the types of experiments that I do. And while some people just go out and enjoy playing easy golf courses, if I’m successful, then I want to be successful on tough courses.”

Zhaohui Xu (pronounced ZHOW-way SHOO) grew up in the city of Suzhou, an hour’s train ride west of the great Chinese port of Shanghai. In his housing complex, families lived close, both physically and emotionally – so close that while his parents were away at their jobs (his father as an engineer in a textile plant, his mother as a teacher of the deaf), an elderly neighbor woman looked after him and his younger brother. And when the doctors said the woman’s breast cancer was beyond treatment, Xu, at age 10, would lie in bed at night and listen to her cry with pain. That was when he decided to become a doctor.

Compassion alone, of course, doesn’t make a career in medicine. As Xu finished high school, he learned that the nation’s best medical college would not admit students from his city that year, but only from Shanghai and Beijing. So, instead of settling for a second-best medical school, he applied for a place in biology at the elite University of Science and Technology of China, thinking he could shift to medicine later.

From his province of 70 million people, 50,000 students took the entrance exam. Xu placed eighth. At the university, he competed with China’s best students in science, including four who had scored first on the entrance exam in their respective provinces. Yet here, too, he did extremely well, ranking second in his class without working terribly hard. “I had this belief in myself,” he says simply. “I think I can catch not-so-obvious things more quickly.”

As he moved from class to class and lab to lab, his ideas about the future changed. In medicine, he would be one doctor helping one person at a time. In bench science, his intellectual gifts might create knowledge applicable by thousand of doctors. “Gradually, I realized that I could learn something that nobody had ever learned before, ” he says. “I could be the first person to discover something or to reveal something or to visualize something. And I think that being the first is a fascinating thing for me – not just repeating what other people have done, but doing something unique, becoming a source of knowledge.”

By 1989, he had decided to pursue advanced studies in the United States. As an undergraduate, he had met vis-
iting American students and teachers and found them to be “ordinary people like us, nothing mysterious about them, very normal.” Despite his contacts with Americans, he knew virtually nothing of life in the U.S. “There was just a sense of curiosity,” he says. “I wanted to go there and see what it looked like.” Armed only with an acceptance letter from the University of Minnesota, Xu boarded an airplane in Shanghai on September 8, 1989. On the flight he slept for many hours. When he awoke, he saw green mountains beneath him, and the enormity of the step he had taken struck him like a blow. “These were not the mountains I was used to seeing. It was a completely different place. I just felt so strange. I really didn’t know what would happen, and I didn’t want to know what would happen.” That night, as the roar of a Los Angeles freeway invaded the room of his nameless hotel, he thought, “Why am I here? I shouldn’t be here. So lonely.”

In Minneapolis, it took long months for Xu to adjust to a new culture. Gradually, he says, “my confidence came back. I knew I could do a great job.” In fact, he took his doctorate in biochemistry in three years, a record for his department. His strengths in chemistry and physics had led him to protein x-ray crystallography, an abstruse and highly technical sector of biological chemistry in which scientists study proteins in crystalline states, examining the spatial relationships of individual atoms in a given protein with extremely high-energy x-rays. From Minnesota, he took his work eastward for postdoctoral study at Yale, where he broke ground in understanding so-called molecular chaperones — molecules that help various proteins to fold themselves into their native structure. In Michigan’s Department of Biological Chemistry, Xu hopes to learn how proteins are moved from one place to another within cells with the help of another class of molecules which he calls molecular “buses.”

At a school of Michigan’s caliber, he notes, he can maintain “scientific sharpness.” The scientist must make many judgments, he says; his fortunes depend on his ability to choose wisely, to capture what is important, what is practical, what are the risks that are worth taking and the risks that are not worth taking. “To be good but not to be overly ambitious,” he says. “Asking the right questions, but not asking the question that cannot be answered.”
“A lot of times, the questions you need to answer and the problems you need to solve are small-scale. It’s not ‘how to cure cancer.’ It’s ‘how do we get this one molecule to do this one thing we want it to do?’ And using your creativity to make that happen is something that I enjoy very much.”

Tom

“Science, is a
“Science,” says Tom Wilson, “is a bunch of toys. And in one way of looking at it, scientists are just a bunch of kids in a toy shop.” Understand that this opinion comes from an explorer of structures that are among the most infinitesimal and unknowable in nature; from a young scientist of whom Peter Ward, M.D., chairman of the Department of Pathology, says, “Dr. Wilson’s work has substantial implications for human diseases,” including cancer.

A bunch of toys? One appreciates the insight only if one believes that play is at the heart of human creativity. Certainly it’s a key to Tom Wilson’s career as a medical scientist. Which started, in a way, with music. He may have been the only kid in the history of Neena-Menasha, Wisconsin, to be told that he played jazz saxophone well enough to make a living at it. “You’d be surprised to find how many scientists are frustrated musicians,” he says. The non-scientist sees the two endeavors as utterly unlike, one “hard” and rational, the other “soft” and whimsical. But there’s common ground between them — the intricacy of the structures, perhaps, or the free play of experimentation, or both. “I suppose you could approach science as a matter of rote and say, ‘What we need to do is apply a set of established techniques to this, that, or the other thing,’” Wilson says. “But there’s no question that the most successful and important scientists have done nothing of the kind.”

As it turned out, he traded the sax for an elite undergraduate program at the University of Wisconsin that guaranteed admission to medical school. Music became his hobby; he taught himself how to play the Celtic-Irish tin whistle, then turned to lutherie, the hand-crafting of stringed instruments. But in medical research he found his true vocation. He searched out a job as an undergraduate assistant in a lab, and here he first saw the appeal of science as a highly challenging game — “to formulate a question, and through your own wits and guile, come up with something which will help you answer that question.”

By the end of four years, Wilson had come to believe he was ill-suited to a career as a pure clinician, though he still wanted an M.D. degree. He switched to Washington University in St. Louis, which offered an M.D.-Ph.D. At first, he saw the latter as supportive of the former. By the time he finished, it was the other way around. “I loved medical school,” he says. “Without the medical training, you miss a lot of what disease is really about. But it also became clear to me that what I liked about medicine was the science — the mechanical aspects of disease.” Through his Ph.D. training, his residence in clinical pathology, and his post-doctoral work (all at Washington University), the study of disease mechanisms led him through ever more minute processes until he was studying the links between the rearrangements of chromosomes and cancer. Scientists have long known that such a link exists. Now Wilson is exploring precisely how one affects the other.

Wilson had a friend in graduate school who gradually tired of medical research in the lab. The process of solving the step-by-step problems of bench research, each of them only a tiny step toward a distant answer, left his friend cold. Wilson found himself having precisely the opposite reaction. Though intent on his ultimate goals, he loved the day-to-day problem solving. “A lot of times, the questions you need to answer and the problems you need to solve are small-scale,” he says. “It’s not ‘how to cure cancer.’ It’s ‘how do we get this one molecule to do this one thing we want it to do?’ And using your creativity to make that happen is something that I enjoy very much.”

That, like the saxophone, is a kind of play — constantly fooling and fiddling not with the keys of a musical instrument but with ideas, even when one’s away from the research bench. “It’s the constancy of being there with (the problem),” Wilson says. “It’s not so much being there in the laboratory, but the science being with you. I would wager that you’re probably going to find that most scientists are like this, that it’s not a 9-to-5 job. It’s all-encompassing. I mean, you are what you’re trying to do in the laboratory. When you’re at a play or playing with your children, it doesn’t go away. When you’re with a problem and spend time with it and work with it so much that eventually it becomes a part of you, that’s when the moments of realization come in.”
At the age of seven, Kathleen Collins informed her parents that she, like her mother, had decided on a career in nursing. “No, no, no,” her father replied. “You need to be a doctor.” It was 1971, before most fathers had learned to talk that way to their daughters. The senior Collins was a school administrator and former English teacher in the small Massachusetts shore town of Norwell. Put your mind to it and you can do whatever you want, he told his daughter. “I really distinctly remember that, so I think it did have an impact on me,” she recalls. “Because of the way I was brought up, I didn’t feel restricted to any particular field. I followed a path based on things I enjoyed and things I seemed to be good at.”

She was very good indeed in science and math, and she nurtured an image of herself as a doctor through the first two years of a pre-med curriculum at Wellesley. Then one of her professors, a biologist named Andrew Webb, invited Collins and
a few other students to help him in his lab. Webb, working with colleagues at nearby MIT, had just cloned a copy of the human gene for interleukin-one, a protein thought to play a major role in activating the human immune system. Collins’ assignment was to clone not just a copy of the gene, but the gene itself.

Month after month, she went to Webb’s lab. As she worked, her conception of science itself changed. Science, she began to realize, was not a settled body of knowledge that one looked up in a book. It was an unfolding mystery — a conversation between investigators and nature in which nature clung jealous to its secrets. And her conception of herself changed, too: “I gained a view of myself as someone who could contribute to better understanding those unknowns.”

In the spring of her senior year, she received acceptance letters from the medical schools at Johns Hopkins and Harvard. She picked up her summa cum laude degree, went home to Norwell and told her parents she didn’t want to go to med school, not yet. She wanted to keep working in Webb’s lab.

“They looked pretty worried,” she says. “But they let me do it.” The next year, she and her colleagues cloned the gene for human interleukin-one. From there it was on to the combined M.D.-Ph.D. program at Hopkins, where she developed an interest in HIV while working with AIDS patients, then to the MIT lab of David Baltimore, the Nobel laureate who is now president of Caltech. Hers was a textbook example of the virtues of combining training in the clinic and the lab. “I enjoyed thinking about virology at the time that the AIDS epidemic was in full bloom,” she says, “and I felt that studying HIV would be an important contribution. A research career studying AIDS, I decided, would nicely combine my research and clinical interests, plus it would allow me to do something I felt was important for society.”

When she describes her work at MIT on a gene involved with HIV called Nef, it becomes clear that Collins, despite the M.D. half of her training, never lost the love of solitary lab work that she discovered at Wellesley. She is a person who chooses words with extraordinary care, but a thrill still resonates in her voice when she describes the night she looked through her microscope and realized that her theory about the Nef gene’s effect on the human immune system was true. “I was working really late, and all of a sudden I saw the answer. I saw that the cells weren’t being killed by the immune system when they expressed this gene, but when we altered the gene so that it wasn’t expressed, the cells were being killed. I was the only one in the world who knew that. That was the best.”

“I was working really late and all of a sudden I saw the answer. I saw that the cells weren’t being killed by the immune system when they expressed this gene, but when we altered the gene so that it wasn’t expressed, the cells were being killed. I was the only one in the world who knew that. That was the best.”
Brian Akerley recalls the exact moment of his first encounter with the fact that DNA exists. It was in a high school science class at St. John’s, a Catholic prep school in Massachusetts. The teacher’s name was Hook. “You remember the person who tells you these things,” he says. Even as a younger kid, he’d had a touch of science fever, demanding that his parents drive him from store to store for chemistry supplies. But his main aim at that early age, he explains with a twinkle in his eye, had merely been bigger and better.

“exothermic reactions” — explosions and fires, that is. But Mr. Hook, drawing open the curtain on DNA, excited a far deeper fascination in the young Akerley.

“You realize that there’s so all of it. And you to do science, I think — you don’t.”

Brian Akerley

“The concept that there’s a molecule that encodes everything, and we can read it — Ha! From then on, I just….” Though Akerley is 33, his voice trails off for an instant, a tiny echo of adolescent wonder still audible. “That molecule — not only does it template all these proteins, but it’s set up in a way that they can direct the entire development process of an organism! That was pretty amazing.”

He went through two years at Bates College telling people he was pre-med, but after just a couple of weeks in the lab of his faculty advisor, the pre-med talk ended. Soon, he was leaving parties at 2 a.m. to run to the lab. “There he goes,” his pre-med buddies would say, “reading that oncogenes textbook again.” He was hooked. Molecular madness. A genetics junkie.

Next came graduate school in immunology and microbiology at UCLA, where his only question about the big city, noted for the glamour of its entertainment industry, was how to find an apartment closer to the lab. For his dissertation, he studied signal transduction in the bacteria...
Seventh Scholar Named

A seventh Biological Sciences Scholar has now been named: Jorge Iñiguez-Lluhí, Ph.D., whose primary appointment will be in the Department of Pharmacology. A native of Mexico City, Iñiguez-Lluhí earned his doctorate at the University of Texas Southwestern Medical Center in Dallas in 1994 and did postdoctoral work at the University of California at San Francisco. His primary research focus is on cellular signal recognition, transduction and response. Five more scholars are expected to be named in the current academic year. The search committee has selected 10 candidates for final consideration from the more than 200 applicants.

*Bordetella pertussis*, which causes upper-respiratory infections. The simplicity of the organism allowed him to trace signal pathways down through the cell to the genetic level. That work led to Akerley’s postdoctoral work at Harvard and now to Michigan, where he continues to study signal transduction in bacteria. Beyond its immediate utility in treating diseases, his work has helped to illuminate the much larger problem of how bacteria exchange information with their host organisms — a basic question that gets to the root of how cells “talk” to one another.

Some variation of the awe that Akerley felt at his “discovery” of DNA probably ignites most scientific careers. But a quality much different from sheer wonder is required to propel such a career over the long haul, Akerley found. Awe comes unbidden; understanding requires repeated acts of intellectual will. Akerley calls the process “demolition and reconstruction” — building up a theoretical structure to explain a natural process, then blowing the structure to smithereens with contrary data, then laying one new brick on another to build a new structure for testing.

“Science is not easy, and in reality it’s not that pretty,” he says. “Scientists have to make it sound good, but it’s hard work.” He’ll be pleased if his work helps lessen the burden of disease. But he can’t honestly say this is more than a pleasant consequence of his obsession. It might even be wrong to say he pushes farther into the genetic mists in pursuit of ultimate understanding. For ultimate understanding is a will-o’-the-wisp, receding even as it beckons the explorer onward. “You realize that there’s so much more to the story that you can’t encompass all of it,” Akerley says. “And you may never know everything. That’s what drives people to do science, I think — the fact that the more you find out, the more you realize you don’t really know what’s going on.”

Yet whenever Akerley and his colleagues break new ground on the far frontier, they’ll leave maps in their wake, maps that will help others toward new cures and new treatments. “Scientists study what’s interesting, not what’s important,” he says. “But what people don’t realize is that later on, what was interesting to a scientist becomes important. If you take an unbiased view, you’re more likely to find something useful than if you tried to grab what you think is useful. It takes a few people figuring out how everything works, and then some other people taking a look at it and finding out what you can do with it. It’s the engineer versus the physicist. If you don’t know what electricity is, it’s going to be very difficult to make a light bulb.”

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A Tradition of Student Generosity and Concern for the Community That Goes Back More Than 70 Years

by Megan Schimpf

The idea for what has become the Galens’ Tag Days was first suggested by Galens member Wall W. Thom at the group’s meeting on November 3, 1927. Funds from the first drive were used for a December party for the children in University Hospital, and a portion was saved to found the Galens Workshop the next spring.

The Workshop, which still exists, offers pediatric patients the opportunity to be more “kid” than patient. Held on the eighth floor of Mott Hospital since the mid-1960s, the Workshop offers events ranging from art projects to Halloween costumes, from parades to parties, from face painting to visits by Michigan collegiate athletes.

Its activities always bring smiles and laughter from Mott patients, which is why hundreds of medical students are willing to give up a weekend every year to collect money to support the Workshop and other activities.

The appearance of Galens members in their red ponchos, standing on Ann Arbor street corners with their buckets on the first weekend in December, is a familiar sight to local residents. “It’s Galens time again,” people say, either preparing to drop coins or paper bills into the buckets or flashing a tag to show they already did. The trademark red and green tags can be seen on almost every winter coat in town that weekend, proud symbols of wanting to help the children of Washtenaw County.

Tag Days is truly one of the highlights of the Galens year. “There is nothing like the sight of 150 medical students in their red ponchos creating a dynamic presence throughout the city,” says Tag Days “czar” Amanda Bauer, a fourth-year student. “When I see thousands of Ann Arborites wearing their colorful tags, I feel a sense of pride and accomplishment knowing the community is with us in our mission.”

Despite the long hours and the often frigid weather, most members come away from the weekend with warm stories to tell — that of the man who gave a hundred-dollar bill, that of the toddler with a few coins, that of the
check for $500, that of the young woman who benefited from Tag Days money as a child, that of the woman who gives money yearly in honor of her father, that of the van with warm food and drinks, that of the personal appreciation expressed for the amount of money collected to help kids.

Financial allocation has also changed since the beginning of Tag Days, with fund distributions also being made to outside groups beginning in the mid-1960s. In 1968, Galens pledged $80,000 to Mott Hospital over 10-12 years for the creation of the Galens Intensive Care Unit for Children. In 1982, however, it was decided that all distributions should be for one year only, and a number of guidelines for giving out Tag Days money were set up — to benefit children younger than 18 in Washtenaw County and for specific projects to organizations that have exhausted all other sources.

“Galens teaches students important skills in community service and fundraising, about making hard decisions using scarce resources,” says Rachel Glick, M.D., associate dean for student programs and clinical assistant professor of psychiatry, who was a Galens member as a student. “It creates a wonderful teaching and learning opportunity for students who choose to join.”

While the first Galens Tag Days raised about $1,000, the 1999 Tag Days collected more than $72,000, augmented by a mail solicitation to alumni/ae, faculty and friends who had made gifts in the past. A large allocation is given every year to Child Life Services at Mott Hospital, but other organizations helping children in Washtenaw County are encouraged to apply for funds as well. Recent allocations have benefited children’s programs at the Hands-On Museum, the Corner Health Center in Ypsilanti, Ozone House, Hope Clinic and the SOS Community Crisis Center.

“Think about this — if you have $10 to give away; it doesn’t feel like much to aid the children of Washtenaw County. But when you donate that money to Galens, you become part of a larger entity that is really making a difference in children’s lives. Your $10 feels like more because you are part of the $2,000 that went toward the new playground at the low-income child care center,” says third-year medical student Victoria Jewell, a three-year Galens member. “I think that Galens promotes the giving spirit in the community by showing people that every little bit helps. Even if you can’t give as much as you would like to, you are still making a difference.”

Red poncho-clad Galens members Elise Georgi (top), Ron Teed (middle) and Shannon Sullivan (bottom) during the 1999 Galens Tag Days, juxtaposed with earlier Tag Days scenes from the Galens photo archives.
Exciting discoveries are going to be made in the biomedical sciences during the twenty-first century, and the University of Michigan Medical School plans to provide many of the scientists who will make them. Educating these future scientists has become an important mission for the U-M, which is carefully monitoring the first class of Ph.D. candidates admitted to the Medical School under the highly collaborative Program in Biomedical Sciences, or PIBS.

The first wave of PIBS recruits arrived in Ann Arbor last fall, a hand-picked contingent of more than 60 graduate students seeking doctoral degrees in 11 programs involving nearly 30 specific research areas under the guidance and supervision of 270 faculty mentors.

We want to produce students who think more broadly. We want to establish a network across disciplines where knowledge and experience can be shared.

Courses of study are tailored to the needs of each student, explains David Engelke, Ph.D., a professor of biological chemistry who is the PIBS program director. “There is no one-size-fits-all curriculum,” he says. “We hope to show them a broad slice of the science that’s out there, while allowing them to specialize as soon as they’re ready.”

The 11 PIBS-sponsored Ph.D. programs include:

- Biological Chemistry
- Biophysics
- Cell and Developmental Biology
- Cellular and Molecular Biology
- Human Genetics
- Immunology
- Microbiology and Immunology
- Neurosciences
- Pathology
- Pharmacology
- Physiology

The notion of combining recruiting, admissions and mentoring aspects of doctoral studies in science isn’t exactly new for the Medical School, Engelke says. Discussions actually began back in the early 1990s, but it took several years of negotiations among faculty and students to smooth out the details and establish the courses of study that eventually evolved into PIBS.

“We began by discussing the need for a common gateway for students interested in biomedical science graduate study,” he says. “That work culminated in what is now known as the Program in Biomedical Science and resulted in the first group of incoming students.”

Engelke is assisted in the overall supervision of PIBS by Associate Director Sally A. Camper, Ph.D., an associate professor in human genetics and internal medicine who is also an associate research scientist in the Reproductive Sciences Program. Assistant Director Mary Chizek and her...
In putting together the first PIBS class, initial recruiting efforts generated 508 applications that resulted in 150 scholarship offers. “We thought we’d get about 33 percent of them,” Engelke recalls. “We ended up with 42 percent, or 66 students instead of 50. It was a very pleasant surprise.”

To compete on a national scale, the U-M as well as its peer institutions offer full financial support, including a stipend for living expenses, for as long as the students are involved in the program. Goldstein says it typically takes five years to earn a Ph.D.

Just as U-M football coach Lloyd Carr and his staff will cross state and international boundaries in the search for the best available players, PIBS recruiters are indefatigable in bringing the brightest scientists to Michigan. “It takes a national advertising effort,” Engelke says. “We have people travelling to colleges and speaking to undergrads in the sciences. With PIBS, we can make the U-M more visible in more places without requiring a separate effort from each program. We also send students, staff and faculty to recruit at seminars. We encourage faculty to talk about the program when they are on the road, and we’ve given them posters to share with friends at other campuses and their alma maters.”

While each of the successful PIBS applicants plans to seek a career in biomedical science, some students begin their first year with more clearly defined goals than others. “People don’t always realize it, but this is one of the largest research institutions in the country,” Engelke says. “Some of the students know exactly what they are looking for, and those are the people we connect with the experts in their areas of interest and then get out of their way.

“Other students are less certain about a specific path, and PIBS is set up to offer broad exposure to many areas and potential mentors. There are classes, research rotations and symposia within the Ph.D. programs. We want to give them a wide exposure to science and allow them to get excited about things they’ve never seen before. After that, they can declare their area of interest and focus there. Or, they may continue through additional rotations. It’s all collaborative,” he says. “We want to produce students who think more broadly. We want to establish a network across disciplines where knowledge and experience can be shared.”

Above all, PIBS candidates are expected to help make major contributions to the overall research efforts of the Medical School. “The role these students play is absolutely vital because they represent the future. As sharp, inquisitive beginners, they continually refresh the research process,” says Joel Swanson, who along with his wife, Michele, came to the U-M three and a half years ago from Harvard and Tufts, respectively. As faculty in the Department of Microbiology and Immunology, both are sharing their knowledge and laboratories as PIBS mentors.

Goldstein is optimistic about the chances of successful Ph.D. candidates finding challenging and rewarding careers in academia, pharmaceutical companies or biotech firms. Or they could even take their scientific expertise to law school for specialized study in patent law, genetics, cell biology, public policy or law enforcement forensics. “We’re training them for a myriad of careers,” Goldstein says. “And,” Engelke adds, “there are an awful lot of niches out there. You just aren’t going to find a lot of people with a science Ph.D. who have to drive cabs for a living.”

staff handle administrative matters and provide daily assistance to students in offices that are already overflowing with applications for the next PIBS class.

Steven Goldstein, M.D., interim associate dean for research and graduate studies and Henry Ruppenthal Family Professor of Orthopaedic Surgery and Bioengineering, who is also a senior research scientist with the Institute of Gerontology, is pleased with the way PIBS has managed to attract highly qualified students while competing directly with similar programs at peer universities. “There is an outstanding pool of candidates out there,” he says. “But we’re in competition with Harvard, Washington University, Princeton and Berkeley, as well as Wisconsin, Yale and the University of Pennsylvania.

“Recruiting is a challenge because there’s a perception that the best work is done on the east and west coasts. But once we get students to visit Michigan, we get a high percentage of them.”

Students Clarise Rivera and Greg DeLassus with PIBS mentor Joel Swanson; below, Associate Director Sally Camper in one of the many laboratories available to PIBS students; at right: David Engelke.
PART II OF III, 1891-1959

In commemoration of Allen Lichter’s appointment as dean last May, the first six deans of the University of Michigan Medical School were remembered in the previous issue of *Medicine at Michigan*. While these forefathers established a solid foundation for medical education at Michigan, there remained a substantial way to go before the Medical School attained its respected status of today. The deans from 1891 to 1959 were instrumental in effecting the transformation from a good medical department to today’s leading institution with its international reputation in medical research and education. The deans during this period initiated clinical and laboratory work, a series of curriculum reforms, dramatically expanded patient care, and strove to inspire higher standards of excellence from their faculty, staff and students.

Prior to 1891 the deans were elected by fellow faculty members, but due primarily to the growth of the University, the board of regents decided that the dean would be appointed by the regents and the president. The first dean of the Medical Department appointed in such a way was bacteriologist and educator Victor Vaughan.

Victor Vaughan’s education and personal qualities gave him solid preparation for assuming a leadership position as dean at the Medical School. Vaughan came from Missouri to Ann Arbor, attracted in part by the University’s excellent chemical laboratory, in 1874. He earned three degrees from the University: an M.S. in 1875, a Ph.D. in 1876 for chemistry, geology and biological studies, and an M.D. in 1878. Vaughan started teaching physiological chemistry in 1876 and held the positions of professor of physiological and pathological chemistry and associate professor of therapeutics and materia medica from 1883-1887.

He and Frederick Novy went to Germany to study bacteriological technique under Robert Koch for a year at the University of Berlin. In 1887 he founded a hygiene laboratory at Michigan, and in that year he became professor of hygiene and physiological chemistry as well as director of the laboratory. He received an honorary LL.D. degree from the University in 1900.

Vaughan's initial research was in medical chemistry. He studied poisons, describing putridine poisoning and becoming such an expert toxicologist that he served as a witness in many criminal and civil trials. Vaughan recognized that “poisoned” milk was caused by bacteria, and in 1885 discovered tyrotoxicon, a poison that forms in dairy products. His research interests then broadened to the nascent field of bacteriology, and included as well sanitation and public health. After his European tour, Vaughan returned to Michigan and instituted the first formal laboratory courses in bacteriology in the U.S. in 1889. He co-founded the Michigan State Board of Health, of which he was chairman for many years.
Beyond his work in medical research and teaching, Vaughan was active in the military, writing extensively on typhoid fever and prevention of communicable diseases. He served as major and surgeon in the Michigan Volunteer Infantry during the Spanish-American War, and upon the outbreak of World War I, Vaughan was appointed to serve under the surgeon general as a colonel in the Medical Corps. In 1919 he was acknowledged with the Distinguished Service Medal for his patriotic service in the war effort.

Vaughan's tenure as dean from 1891 to 1921 had a tremendous impact on the development and improvement of the University of Michigan Medical School. He worked diligently to recruit research-minded faculty from around the country with the attitude that “Medicine is a live, growing science, and no one is entitled to hold a chair in a…medical school who is not a contributor to the growth and development of his specialty.” [Kenneth M. Ludmerer, “The University of Michigan Medical School: A Tradition of Leadership,” Medical Lives & Scientific Medicine at Michigan, 1891-1969, ed. Joel D. Howell (Ann Arbor: The University of Michigan Press, 1993), p. 21.] In the tradition of his predecessors Abram Sager, Silas Douglas and Alonzo Palmer, Vaughan valued a curriculum that combined basic science and clinical practice. Vaughan also helped raise admission requirements, instituted a longer period of instruction, and emphasized the importance of having a comprehensive library.

Vaughan was agreeable, relaxed, soft-spoken, and determined to improve the standards of medicine at Michigan, encouraging both students and faculty to conduct research. He was revered as a leader, teacher, and researcher, and his leadership made Michigan a paragon of modern medical education. He retired emeritus from the University of Michigan in 1921, and died eight years later.

Succeeding Victor Vaughan as dean was Hugh Cabot, a colorful and controversial figure. Called visionary by some, tyrannical by others, Cabot accomplished much as dean and had a remarkable academic career. He challenged the status quo to bring change and innovation to the University of Michigan Medical School.

Hugh Cabot had developed a successful professional life before he came to Michigan. He completed his A.B. and M.D. degrees at Harvard University, where he was assistant professor of surgery from 1912 to 1918, and professor of surgery from 1918 to 1919. He interned in the Surgery Department of Massachusetts General Hospital, specializing in urological surgery. Cabot spent most of his time teaching and performing surgery rather than conducting research. He wrote Modern Urology in 1918 and was one of the first to suggest that urology ought to be a distinct specialty.

At Harvard, Cabot organized a medical unit before the United States entered World War I, and from 1916 to 1919 he was honorary lieutenant-colonel in the Royal Army Medical Corps in France. When he returned from the war he found that his private practice had practically vanished, so he decided to accept the U-M Medical School’s offer to be a new “full time” professor. Cabot thought Michigan would be more progressive than his home state of Massachusetts since it had a university subsidized by taxes and a shorter, less restrictive tradition. Cabot was interested in making quality health care affordable for the average citizen, and envisioned a health care system with full-time, hospital-based group practices where patients would pay according to their means. He strongly believed that medicine was a profession that required scientific education and should benefit humankind—that it was not simply a trade with monetary gain as a primary interest. Seeking change and new opportunities, Cabot left conservative Boston at age 47 to join the University of Michigan as professor of surgery in 1919.

Cabot had a strong influence at the University of Michigan as a teacher and as dean. He was a good speaker who gave vivid, interesting lectures, and he was dedicated to maintaining high...
standards of academic performance. Cabot’s protégés included Reed Nesbit and Nobel Prize winner Charles Huggins. He was chair of the department of surgery and head of the section of urological surgery. When Cabot was appointed dean in 1921, many faculty members had recently left the surgery department because of the structural reorganization from part-time to full-time teaching positions. This gave Cabot the opportunity to build a new department, so he hired Frederick Coller, Leroy Abbott and John Alexander, all eminent specialists. At this same time, specialties within the department were differentiated into general, orthopedic, neurosurgery, urological, and thoracic sections.

Cabot also oversaw the completion and staffing of the new University Hospital on Ann Street, the East Medical Building and the Simpson Memorial Institute. Also during Cabot’s tenure, the Department of Biological Chemistry was established, and most departments had graduate-level training programs. In accordance with a resolution passed in 1921 by the state legislature, Cabot effected the closing of the Homeopathic Medical College by combining it with the “regular” medical school.

While Cabot was accomplished as dean, some of his actions caused members of the faculty to hold him in high disfavor. Cabot was described by one of his trainees, Henry K. Ransom, as “short and stocky in build with a sturdy physique, a brusque manner and a domineering attitude.” [H. K. Ransom, “The Department of Surgery of the University of Michigan during the Cabot Administration (1919-1930)” (Internal document, University of Michigan Department of Surgery), p. 4.] It has been suggested that the influence of American philosopher Ralph Waldo Emerson, a friend of Cabot’s father present during his formative years, fostered Cabot’s tendency to speak honestly and directly — sometimes at the risk of his personal relationships.

Aggravating an already unstable dynamic at the Medical School was Cabot’s confrontation of the ongoing issue of part-time faculty seeing private patients. Cabot disapproved of professors who put a lot of time and attention into their private practice but neglected their teaching and hospital responsibilities. Cabot’s aforementioned economic ideology and support of a full-time faculty threatened private practitioners, who eventually aligned with the Michigan State Medical Society to formally oppose the “full-time” method at the hospital. Cabot held steadfast in his principles, but in order to assuage the unrest, the regents requested Cabot’s resignation early in 1930. His dedication and integrity did leave a positive mark, however, as many of his innovative policies were quietly accepted by the Medical School decades later.

After Hugh Cabot’s departure, the administration at the Medical School went through a transitional period. Instead of immediately appointing another dean, the regents selected an Executive Committee of five faculty members. The original Committee was formed midway through the 1929-1930 academic year, consisting of James Bruce, G. Carl Huber, Frederick Novy, Max Peet, and Udo Wile, with President Ruthven as chairman, ex officio. The following academic year Harley A. Haynes and assistant professor Arthur C. Curtis replaced Huber and Peet, and Frederick Novy became chairman of the committee. The Executive Committee directed the affairs of the school from 1930 to 1933, overseeing the appointment of five new department chairmen and the addition of two new floors to the hospital. The Executive Committee still exists today with the dean as chair.

James D. Bruce served on the Executive Committee as director of postgraduate medicine. He earned his M.D. degree from the Detroit Medical College in 1896, and practiced for eight years before starting his graduate studies at the U-M Medical School. He was an assistant in the Department of Internal Medicine, and practiced general medicine and surgery in Saginaw from 1906 to 1925. Bruce served in the U.S. Army Medical Corps in France during World War I, and from 1923 to 1934 his was councilor of the Michigan State Medical Society. Believing that standards of medical service needed to improve, Bruce gave up his private practice to lead the Department of Internal Medicine at Michigan. In 1931 he was appointed vice-president in charge of university relations, a position he held until retiring as vice president emeritus in 1942. Bruce strongly supported continuing education for physicians and helped create medical teaching centers around the state.

Udo J. Wile served as director of clinical medicine on the Executive Committee. Wile became professor of dermatology at the age of 28 and was at the time the youngest member of the medical faculty ever to be given the rank of professor and chairman of the department. He had studied with distinguished physicians and researchers in Europe, and enjoyed an encyclopedic knowledge of dermatology. Albert Furstenberg, later dean of the Medical School, related this story about Wile:

When he [Wile] arrived in town he looked a little timid and embarrassed. Some of the older faculty members thought they would have some fun with him. They told him that at the annual convocation that marked the opening of the Medical School, he would be expected to give an inspiring extemporaneous speech. Naturally, he went to the convocation with fear and trembling and was miserable throughout the exercises. Finally, when all of the events of the program were over, Dean Victor C.
Vaughan arose and said, "My Christian friends, students of the Medical School, it now becomes my privilege and pleasure to introduce a new member of the medical faculty. I shall not ask him to speak. I merely want him to stand up so that you will not mistake him for a freshman." [Albert C. Furstenberg, "My Teachers in the Medical School," Our Michigan: An Anthology Celebrating the University of Michigan’s Sesquicentennial, ed. Erich A. Walter (Ann Arbor: University of Michigan, 1966), pp. 43-50.]

Having survived this mild hazing, Wile proved to be a valuable faculty member and became chairman of the Department of Dermatology. He clearly showed his students how medical knowledge applied to clinical problems, and Albert Furstenberg wrote that he created "a measure of leadership in our programs of undergraduate and graduate medical education." [Ibid.] He was optimistic, had genuine concern for the welfare of his patients, and received respect and admiration from his students and colleagues.

Harley A. Haynes, director of the University Hospital, brought economic savvy paired with medical experience to the Executive Committee. Earlier in his career, he was a clerk in the auditor’s office of the Central Vermont Railroad. He redirected his interests toward medicine, and received his medical degree from the University of Michigan in 1902. He completed a surgical internship in the University Hospital from 1902 to 1903, and was resident physician at the Michigan Reformatory in Ionia. In 1924 Haynes was named director of University Hospital, holding the position until he retired as director emeritus in 1945. He was one of the first to introduce cost accounting to hospital administration. Besides working as a physician and administrator, Haynes later became president of the State Savings Bank of Ann Arbor, and a director of the Michigan Consolidated Gas Company in Detroit.

Also a member of the Executive Committee was Arthur C. Curtis, secretary of the Medical School. Curtis graduated from the U-M Medical School in 1925, interned at University Hospital, and moved his way up the ranks from instructor of internal medicine in 1928 to associate professor in 1935. In 1941 he started postgraduate training at the Mayo Clinic, and returned to the University of Michigan in 1942 to be professor of dermatology. Curtis was chairman of the Department of Dermatology from 1946-1967, and served on numerous professional organizations, including the American Board of Dermatology, of which he was president. Curtis became a world-renowned dermatologist, and had a lifelong dedication to medicine at the University of Michigan.

The chairman of the Executive Committee and director of pre-clinical medicine was Frederick G. Novy, who was formally appointed dean in 1933. He held a brief two-year tenure as dean, but throughout his long career he made a great contribution to the Medical School. As a boy, he had saved money to buy a microscope, which he had used to study samples from nearby swamps. Novy went on to study at the University of Michigan, where he received four degrees: a B.S. in chemistry in 1886, an M.S. in 1887, a Sc.D. in 1890, and an M.D. in 1891. He went to Europe with Victor Vaughan to study in the laboratories of Pasteur and Koch and to purchase equipment for use in a bacteriology course. Novy’s class was so successful that it became a requirement for students in the Medical School. In 1902 he became professor of bacteriology, heading the department from 1902 to 1935.

Novy was an accomplished and innovative researcher, and his work truly spanned bacteriology, protozoology, virology, and immunology. He was one of the first to demonstrate anaphylatoxin, a histamine, which laid groundwork for future developments in antihistamines. He discovered one of the two organisms that causes gas gangrene, known later as Novy’s bacillus, and invented laboratory tools such as the Novy coverslip forceps and the Novy anaerobe jar. Novy was on the Michigan Board of Health from 1897 to 1899, and with Victor Vaughan helped educate the public about the germ theory of disease, food poisoning, disinfection, and control of communicable diseases such as diphtheria and typhoid fever. He was a member of the U.S. Commission to Study Bubonic Plague in San Francisco, California, in 1901, and treated a case of pneumonia plague in a University student. He received the honorary LL.D. degree from the University of Michigan in 1936.

Frederick Novy was loved and respected by colleagues and students, and even in his 22 years of retirement, he was sought as an expert authority and counselor. He had a colorful personality, which Sinclair Lewis drew on for the character of Dr. Gottlieb in his highly popular ➤
Following the retirement of Novy, Albert C. Furstenberg was appointed dean in 1935. Furstenberg served 24 years as dean, and his stable yet enthusiastic leadership propelled the U-M Medical School into a fully modern institution. A Michigan native, Furstenberg showed an interest in medicine even at the young age of eight by accompanying a local physician on house calls. Later he attended the University of Michigan, earning his B.S. in 1913 and his M.D. in 1915. From 1915 to 1916 he held an internship at University Hospital, and started a practice in Ann Arbor which he kept until his retirement in 1965. Furstenberg specialized in otolaryngology, and he conducted research on the fascial planes of the neck and neurology of the ear, nose, and larynx. He also studied Meniere’s disease, osteomyelitis of the skull, and conductive deafness, and wrote numerous papers.

In 1918 Furstenberg became instructor of otolaryngology, and he moved his way up the ranks to chairman of the department in 1932. His teaching at Michigan earned him much respect and admiration. He was a great lecturer and teacher, and cared enough about his students to become personal friends to many of them. He encouraged and advised his students by telling them, that if they were willing to devote their lives to it, medicine would be a better way of life than any other.

In 1935, Furstenberg was appointed dean. He proved to be an excellent leader and energetic administrator, always thinking ahead to the future of the Medical School. He made considerable effort to expand and improve the facilities, achieving great success. During his tenure as dean, the University of Michigan Medical School became the largest in the country. Classes were expanded to 200 students, and Furstenberg helped select outstanding teachers and scientists for the faculty. Since former dean Hugh Cabot did not especially promote research at the Medical School, Furstenberg helped revitalize this aspect of medical education at Michigan. Michigan became a premier medical research institution, and facilities were expanded thanks to government and private funds. Furstenberg’s ongoing friendships with philanthropists Sebastian Kresge and Charles Stewart Mott helped facilitate their financial contributions to the Medical Center. Their substantial gifts helped establish the Kresge Research Building in 1953, the Kresge Library in 1955, the Institute of Industrial Health in 1957, the Kresge Hearing Research Institute in 1962, and the C.S. Mott Children’s Hospital in 1969.

An example of Furstenberg’s excellent leadership capabilities was his response to national need during World War II. Furstenberg had some military experience, having served as 1st Lieutenant with the U.S. Army Medical Reserve Corps in Ann Arbor during World War I, and as consultant to the Office of the Surgeon General of the Army during World War II. When a shortage of physicians developed during World War II, Furstenberg temporarily accelerated the medical program at Michigan.

In addition to his other accomplishments, Furstenberg was the National Research Council subcommittee chairman, and an honorary member of the Army Medical Library. His distinguished career was recognized with many professional honors, and in 1960 he was named dean emeritus. He died in Ann Arbor in 1969.

Furstenberg was the last dean to divide his time between departmental administration, private practice, and direction of the Medical School. William Hubbard became the first full-time dean in 1959. This new era of leadership leading up to the present will be explored in the next issue of Medicine at Michigan, in conclusion of this three-part series on the history of the deans of the University of Michigan Medical School.

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Teresa Black, an Ann Arbor native, is a recent graduate, in anthropology, of New York University.
When the 298th General Hospital was called to active duty in June of 1942, the University of Michigan Medical School's organization of the unit already had been two years underway. The 298th provided heroic front-line medical services to the armed forces in England, Belgium and France under the command of Lieutenant Colonel Walter G. Maddock, M.D., associate professor of surgery, with nurses directed by Lieutenant Margaret K. Schafer, instructor in nursing and operating room supervisor who ultimately became lieutenant colonel and chief nurse in the European Theater of Operations.

The 298th was one of the countless contributions made by the University to the nation’s defense during perhaps the most challenging period of its history. To meet the demand for trained personnel, the University moved to a three-term year for continuous operation, and the Medical School accelerated its instruction to produce doctors in three years instead of four.

Unprecedented levels of government research, much of it classified, were conducted at the University, and the U-M trained more than 4,000 enlisted men and officers for the Navy, 8,000 Army soldiers, and 12,350 civilians in such areas as language instruction, ordnance inspection, meteorology, naval architecture and Army law—all while the University itself suffered a severe shortage of workers due to massive conscription and voluntary service.

Burgeoning enrollments as veterans returned challenged the University after World War II as well. Older than the typical student, often married and more likely to have cars, the surge of veterans changed the student landscape forever and helped signal a post-war University far different from that which existed before the conflict.
Many of the names most closely associated with the more contemporary history of the school are names that have a child’s meaning for her: of Roy Bishop Canfield, for instance, whose premature death in a car crash led to her father’s appointment as chair of the Department of Otolaryngology, she remembers staying overnight at the Canfields’ house, and “hating it—they had satin sheets and I kept sliding out of bed.”

Her father and Alexander Ruthven (president of the University from 1929 to 1951), whose families enjoyed a close friendship for more than 20 years, shared an interest in horseback riding, and she remembers spending weekends on the farm they bought together near Dexter and the summers the families spent in adjoining cottages on the shore of Lake Michigan near Frankfurt.

“...he was never interested in genealogy. He used to say, ‘You are what you make of yourself, not what you’re from.’”

Her parents’ marriage derived from a medical event: her mother, Elizabeth (known as Micky), a young college student at the time, was a diphtheria patient in the old Infectious Diseases Hospital when she met her future husband, the attending physician. “They couldn’t have been more different,” Furstenberg says. “My mother was a freshman, social, outgoing, dramatic, artistic. But my father had the good sense to know she would be one of his greatest assets.” Micky earned her bachelor’s degree from Michigan four years after her husband became dean of the Medical School, and Nancy remembers her father “standing up and bowing” as his wife received her diploma.

Although her forthrightness and outgoing personality Nancy Furstenberg attributes to her mother’s genes, she carries with her a heavy dose of her father’s down-to-earth pragmatism. “I wanted to be an actress,” she says. “I spent time at Interlochen and I got accepted into the Yale School of Drama, almost the same day I got accepted into the University of Wisconsin Medical School. But I didn’t have high cheekbones and I didn’t have a great figure, and I said to myself, ‘Get real.’ I’ve never regretted the choice I made, though I do wish I could have been more successful in my own medical career while Dad was still alive.” (After her father’s death she went on to become associate dean of the Medical School at the University of North Dakota.) She does remember with satisfaction, though, the time she overhead him say on the telephone to a colleague, “I used to wonder about women in medicine, but Nan seems to be doing all right.”

Now in her 70s and again a resident of Ann Arbor, Nancy Furstenberg retains the abiding interest in medicine that began in her early childhood. “I think my first word was ‘oto-rhino-laryngology,’” she laughs. As the Medical School celebrates its sesquicentennial, she herself celebrates her life as a physician and medicine’s promise on the eve of revolutionary new advances in the life sciences. “I’ve always been more interested in the future than in the past,” she says. “I got that from my dad; he was never interested in genealogy. He used to say, ‘You are what you make of yourself, not what you’re from.’”

**The Furstenberg Era**

**Nancy Furstenberg Remembers Her Father**

Her father also pursued outreach programs with hospitals in Flint, Detroit and Grand Rapids, Nancy says, hoping that by doing so students would gain a more realistic and varied clinical experience. He was an original member of the federal government’s Dean’s Planning Committee, advocating for a linkage between medical schools and the Veterans Administration hospitals as a means of improving medical care for veterans returning from World War II and expanding the clinical experiences available to students.

One of her father’s major contributions to the Medical School, she says, was his ability to raise funds for important new construction and programs, an achievement that resulted mainly from the friendships he had built in the 1930s with such people as philanthropists Sebastian Kresge, W.K. Kellogg, and C.S. Mott. “My father was extremely good at convincing them that the school was their school, that they were partners in the enterprise, and that therefore they should provide more money to accomplish its goals,” she says.

“My father was extremely good at convincing them that the school was their school, that they were partners in the enterprise, and that therefore they should provide more money to accomplish its goals.”

Her father’s commitment to building those relationships drew the entire family into the effort on many occasions, she recalls. “Our whole family and the Ruthvens went out to Palm Springs once to visit W.K. Kellogg,” she recalls. “I remember hearing my father and President Ruthven whispering together about the alarmingly high cost of our hotel rooms: $35 a night. They were both frugal. But it was well worth it. Kellogg even named one of his Arabian horses after Dad.”

Nancy Furstenberg’s memories of the University of Michigan and the Medical School derive from several perspectives: that of a young child growing up in Ann Arbor as the daughter of a physician who later became dean of the Medical School; an undergraduate at Michigan majoring in English; and, later, a resident in internal medicine (her interest was diseases of the lung, especially tuberculosis) in the Medical School where she was subsequently a member of the faculty for 16 years.

...continued on back &gt;
When Eric Kaldjian (M.D. 1989, Residency 1994) and his brother Lauris (M.D. 1989), who is a year younger than he, received their medical degrees from the University of Michigan Medical School in 1989, they had both the future and the past on their minds. Their tassels and gowns were symbols of the careers they envisioned in medicine and science – Eric is now director of pathobiology in worldwide preclinical safety at Parke-Davis in Ann Arbor; Lauris is pursuing a doctorate in medical ethics at Yale University.

The little yellow buttons (Beat the Ball!) they had attached to their gowns pointed to an interest in the past. Specifically: the past symbolized by Old Main, the main University hospital in which generations of physicians like Eric and Lauris trained from the years 1925-1986.

While they recognized that the outdated hospital had to go, they wanted to save at least part of it, and most especially the huge Albert Kahn-designed entry arch fronting on Observatory Street. They were not alone: Richard Judge, M.D., a member of the cardiology faculty, and Nicholas Steneck, Ph.D., a U-M history professor, were part of the group leading the fight to save the arch, carved from blocks of Indiana limestone.

Yellowed Ann Arbor News clippings saved by Eric at the time chronicle the effort: (“U-M urged to save Old Main,” “A last-minute appeal to save part of Old Main,” “Arch of triumph wins reprieve,” “Entry arch will live on as tribute.”)

Eric is very pleased that the Medical Center Alumni Society is now asking alumni/ae to contribute gifts to support the reconstruction of the arch in approximately the same place where it once stood. The plan calls for a plaza to be constructed to support the arch, and those who contribute gifts of $1,000 or more will have their names permanently inscribed at the site.

For more information about making a gift, alumni/ae may call the office of the Medical Center Alumni Society at 998-7705.
The old Beatles classic, “When I’m Sixty-Four,” imagined old age to be about half of what today’s scientists are imagining old age to be. But despite the optimism of researchers like Richard Miller at the University of Michigan, the song lyrics don’t have to be rewritten yet.

What causes aging? What, if anything, can cure aging or slow it down? Although aging affects all who live long enough, and although it has a huge impact on nearly all disease, especially common killers like cancer and heart disease, its cause and cure—if any is indeed possible—remain a mystery.

But Richard Miller, M.D., Ph.D., senior research scientist in the Institute of Gerontology and professor of pathology, thinks that finding the cause, and perhaps even the cure, for aging is feasible and that the results may very well be spectacular at some time in the future. “It’s certainly possible that aging research could lead to a 50 percent extension in the human life span,” he says, “but we are definitely not yet close to knowing how.”

His research has focused on finding some of the clues that may bring us closer to solving the mystery of aging. Miller has been a leading researcher in this area for the past two decades, specializing in the genetics of aging and aging’s effects on the immune system, as well as in the effort to understand what controls the rate of aging.

**A single aging clock**

Although it’s not the most popular view in the field, Miller believes strongly that aging is a unified process, that there is a single “aging clock” that times the aging process, at least in mammals. “Aging is a process that involves the whole organism, not just a single organ system, just as development is,” Miller emphasizes, “although of course aging is as different from development as the process of manufacturing a car is from the process of turning new cars into rust buckets.”

Miller argues that there are a number of strong lines of evidence for the existence of a single aging process or clock, even though we don’t have any real idea what that clock is. One type of evidence comes from evolution, both between species and within species. “We know that there are differences in rates of aging between different species. But if there were many different aging processes, controlled by many different genes, it would be hard to see how these could evolve,” Miller contends.
“For example, if a gene just postponed one form of cancer, it would have hardly any effect on an animal’s life expectancy and its ability to survive. There must be a relatively small number of genes that control some central rate process to enable species to live significantly longer than their ancestors.”

To give one example of how dramatic rate differences can exist between species, Miller points to the difference in tumor genesis rates between mice and humans. A given group of cells in a mouse is 100,000 times more likely to develop into a tumor than the same-sized group in a human in a given length of time. Similarly dramatic rate changes have to occur in many other aging processes to allow the much larger human to live 50 times longer than a mouse.

Considerable changes in rate of aging can happen in relatively short spans of time, again indicating that a few genes regulating a central rate process are at work. For example, Miller points out, an isolated group of opossums in Virginia decreased their aging rate by a factor of two in only a few thousand generations. Within species, too, differences in aging rates can be
Ten years later, he’s pleased that he’s established a national reputation as a “gait guy” (also a “fall guy”) and that he and his biomechanician collaborators, as he calls them, were able to contribute a chapter to a major geriatrics textbook, *Principles of Geriatric Medicine and Gerontology* (McGraw Hill, 1994), establishing themselves as major movers in the area of geriatric mobility.

The subject of mobility and aging, and the consequences of time, life habits and disease, is not as simple as it might at first seem. “There is an accumulation of things over which you may or may not have control,” Alexander says. And then there’s the whole psychological component of aging, one not to be taken lightly in a youth-obsessed culture. “We want to start looking at people in their peri-menopausal years—their 40s, 50s, 60s,” he says. “Our theory, based on some anecdotal observations, is that they start giving up stuff. They express expectations of frailty and decline.” And, of course, there are the catastrophic events that people fear as they grow older, the strokes and hip fractures that cause, at least temporarily, sharp declines in mobility, that, at best, level out to the earlier rates of slower decline.

The focus of Alexander’s research, really, is to understand the mechanisms that determine whether or not a person can maintain good mobility as they age, and, at least, as he puts it, help to “make a dent in the slow slide.” When he looks at an act as clear-cut as getting in and out of a chair, Alexander now sees a sea of complexity involving not only the biomechanics of such an act, but the cognitive piece as well, which speaks to such factors as memory, affect, mental flexibility and visual/spatial acuity. And then there’s the chair itself, which falls into the large category of “environment.”

Alexander is keeping an open mind about what might work. He and his team are now proposing to add to their catalogue of potential “saves” such regimens as aerobic training, balance training and tai chi to see if they might help. Tap dancing perhaps? He doesn’t have that on the list, but he is presently developing ways to assess and train rapid foot movement to determine whether rapid stepping is important in maintaining mobility.

At the moment he and his team have plenty of analysis ahead of them. “We’re drowning in data right now,” he says. “But we hope before long we’ll have some good solid answers that will make a difference in the way people move and keep moving as they age.” If Alexander succeeds in his work, those 120-year-olds of the future may not be playing tennis — but they won’t be falling down either.
dramatic: some breeds of dogs can live, on average, 50 percent longer than others, although they are all the same species so must share all but a relatively few genes.

How could such genes that regulate the rate of aging evolve? Citing ideas and work by Peter Medawar (the late Nobel Prize-winning English zoologist noted for his work in immunology) and others, Miller contends that environments that pose a high risk of mortality to animals naturally favor genes that allow for quick development and high rates of reproduction, even if this, as a byproduct, causes increased rates of aging in older animals.

“Think about a population of mice living in a tough neighborhood filled with owls, cats and mouse viruses, where mice generally don’t live to a ripe old age,” he says. “A gene that postpones aging in 18-month-old mice, but at the same time slightly impairs fertility or retards the age of the first litter, will be strongly selected against, while genes that do the opposite will be strongly selected for. There just are not many 18-month-old mice around to benefit from retarded aging. The result is mice who, when preserved from predation and infection, age rapidly after 18 months.”

Human beings, too, have been subjected to much the same pressures during nearly all of our history. For most of that time, people were struck down, mainly by infectious disease, at a steady rate of two or three percent a year, almost regardless of age once they survived infancy, leading to a life expectancy of 25-35 years. Only a quarter or less of the population that survived could expect to reach 50 (as compared with more than 90 percent in the U.S. today) and only 10 percent would reach age 70. Genes that promoted slower aging after 50 and especially after 70 would tend to be swamped if they adversely affected the reproductive capacity of the much larger numbers of 20-30-year-olds, so it should not be surprising that aging makes it difficult for people to survive more than about twice as long as our ancestors did.

Another strong argument for a single aging clock comes from the well known fact that reduction of caloric intake in rodents can slow aging, extending life spans by as much as 50 percent. As was discovered 50 years ago, rats and mice fed well balanced diets with 50 percent less calories than they would eat if given free access to food, live half again as long, remaining healthy and very active long after their well-fed cousins have passed on. “Consuming fewer calories retards equally nearly every sign and symptom of aging,” Miller points out, “with effects on cells that divide, cells that never divide, protein changes, disease rates, as well as mortality. To assume that each of these is the result of an effect on a separate aging process seems to me to flout Ockham’s Razor. Clearly caloric restriction is somehow affecting a central aging process.” (Ockham’s Razor is the principle credited to medieval philosopher William of Ockham, which suggests that the simplest explanation consistent with all observations is the best.)

“Clearly caloric restriction is somehow affecting a central aging process.”
—Richard Miller

A “cure” for aging?
The idea that aging is controlled by a single clock has one very important implication—that potentially the clock’s rate can be changed and aging slowed down, perhaps significantly. “We know that evolution can change life spans radically and swiftly,” says Miller. “Take some mice to a tropical island paradise, free from predators and pathogens and a gene that slows the aging process even at the expense of say, smaller litters, rapidly takes hold. Evolution has done the trick many times.” In addition, we know that caloric reduction and other
somewhat less drastic environmental modifications can also reset the aging clock. So the prospect of the extension of human life and the slowing of the aging process by even 50 percent is not out of the question, Miller believes.

A “cure” for aging or a way to slow it down would also radically reduce all forms of disease, Miller points out. Indeed, without retardation of the aging process, it will be very difficult for medical science to continue to improve human life expectancies as it has done in the past. To give some perspective on this, look at the history of human longevity. From the Middle Ages all the way up to 1930 in the United States, improvements in nutrition, public health, housing and working conditions slashed the mortality rate for those under 50 by more than four-fold and for those 50-70 years old by half, leading to an increase in life expectancy at birth from 35 years to 60 years. From 1930 to 1950, antibiotics attacked the ancient scourge of infectious disease and further improvements in living standards knocked under-70 mortality rates down by another factor of 1.6, adding almost a decade (8.4 years) to U.S. life expectancies.

But since 1950, gains have come much more slowly. Despite all the medical advances of the past half century, only 7.4 years have been added to U.S. life expectancy, even with under-70 mortality rates still dropping by about one percent per year for most of that time. Part of this slowdown may well have to do with societal factors. Life expectancies for African Americans, for example, have nearly stagnated since the mid-1980s at levels reached 40 years earlier for Americans of European descent, presumably for reasons unrelated to medical research advances.

But another major factor in the slowing of increase in human life span is the difficulty of reducing mortality rates among those over 70. While a person under 50 has only five percent the mortality rate of a same-aged ancestor in the Middle Ages, a modern 70-80-year-old has 60 percent the mortality rate of his similarly aged medieval ancestor—or, for that matter, of similarly aged well-to-do Romans. Without discoveries that retard the aging process itself, mortality rates in the elderly will continue to be difficult to change, thus preventing future increase in life expectancy.

**Telomeres are not the answer**

If there is an aging clock, where is it located and what is its nature? One place that Miller strongly believes the clock will not be found is in the telomeres at the end of human chromosomes, despite the large amount of publicity such repetitive sequences have had in mass media reports recently. Interest in telomeres originated ultimately in studies done more than 50 years ago that indicated that human fibroblasts would undergo no more than about 50 doublings in cell cultures. Such a “Hayflick limit” was observed to grow shorter with cells from older individuals, inspiring the hypothesis that aging was the result of an inherent limit in the number of times that human cells can undergo division. (Leonard Hayflick is a cell biologist at the University of California-San Francisco who first noted that human cells grown in tissue culture will only divide a certain number of times.) Later it was discovered that the length of telomeres tended to be less in older animals and humans and that telomere length remained constant in cancer cells, which can replicate indefinitely. The conclusion was that telomeres were the aging clock, slowly counting down the number of divisions cells had left.

In 1998 this hypothesis led to a flurry of public attention when researchers engineered cells that maintained their telomere length, could replicate indefinitely in vitro and were not cancerous. As articles in the mass media multiplied like dividing cells, other researchers speculated that “immortalized” cells could be reintroduced into the human body to rejuvenate organs and perhaps slow the whole aging process. ➤
Last fall was the tenth anniversary of the establishment, at the University of Michigan, of the nation’s first Claude D. Pepper Older Americans Independence Center. The Center was initially funded with a $6.1 million grant from the National Institute of Aging to advance research on health care problems of the elderly and to train future academic leaders in geriatrics. A recent, successfully competitive renewal grant will continue funding for the Center through 2004. (Claude Pepper [1900-1989] was a U.S. senator and congressman from the state of Florida. A confidant of President Franklin Roosevelt, he led the fight to bring the U.S. into the Allied effort in World War II. The ranking Democrat on the House Select Committee on Aging when it was created in 1975, he became a powerful advocate for older Americans, crusading for the strengthening of the Social Security system and Medicare, and against involuntary retirement, age discrimination and abuse of the elderly.)

The Pepper grant supports research within the U-M Geriatrics Center in basic science, clinical science and health services research dedicated to improving the health of older adults. Jeffrey B. Halter, M.D., is program director of the Pepper Center and director of the U-M Geriatrics Center. Research programs funded by the Pepper grant at Michigan are in four areas:

- **Homeostasis.** Coordinator is Jeffrey B. Halter, M.D. Homeostasis refers to the internal control mechanisms that regulate important body functions such as blood pressure, metabolism and temperature. Of particular interest at Michigan are diabetes mellitus and its complications, altered blood pressure regulation, and immune system defense and response to injury.

- **Cognitive Function.** Coordinator is Roger Albin, M.D. Cognitive function focuses on the study of the aging nervous system. Scientists engaged in this area of research interact with scientists in the Michigan Alzheimer’s Disease Research Center, one of 15 centers established by the National Institute of Aging, and the Center for Applied Cognitive Research on Aging, which focuses on neuropsychological effects of aging.

- **Physical Function.** Coordinator is James Ashton-Miller, Ph.D. This research addresses problems of impaired mobility, including underlying molecular biological mechanisms, the role of coordination, skeletal muscles, bones and joints, and the biomechanics of movement.

- **Health and Well Being.** Coordinator is William Weissert, Ph.D. Research in this area focuses on such issues as comparative health, successful aging, health policy and health systems, and health behavior and education.

The Pepper Center also includes four “research resources cores” to support U-M geriatrics research, and a “research development core” specifically designed to help train junior faculty in geriatrics research.

The National Institute of Aging also supports many other centers at the U-M for research on aging, including the Alzheimer’s Disease Research Center, the Nathan Shock Center for the Biology of Aging (molecular and cellular mechanisms of the basic biology of aging), the Michigan Center on the Demography of Aging, the Center for Applied Cognitive Research on Aging, and the Michigan Center for Urban African American Aging Research. In addition, funding from the National Institutes of Health supports the Alcohol Research Center and studies of alcoholism in the elderly.

The State of Michigan has supported aging research at the University of Michigan since 1965, when it established the Institute of Gerontology at the U-M. One of the oldest and most highly regarded academic programs of its kind, the Institute’s public mandate to pursue research, education, and public service related to aging has resulted in a large number of graduate courses and faculty-initiated research projects. The Institute is a major research resource, encompassing biomedical and social sciences and their interdisciplinary interaction in studying the aging process. The Institute provides research training in gerontology for pre- and post-doctoral students, including all fellows in geriatric medicine. Ari Gafni, Ph.D., is director of the Institute and Jeffrey Halter is medical director.
Miller (as well as many other aging researchers) is extremely skeptical that the new data tell us much about aging. “This is interesting research but I don’t think it has anything to do with the real aging process,” he says. First of all, Hayflick’s observation which drew a correlation between age and cell division was based on cells growing in the alien environment of a test tube, and while there were many cell types in the body for which cell division is limited—nerve cells, of course, and probably fibroblasts as well—there’s no reason to think that these growth limitations contribute to aging in the whole organism. The Hayflick limit is 50 or so cell divisions, but intestinal epithelium cells undergo thousands of divisions in a human or mouse lifetime. Conversely, human neuron cells, which do not divide at all in adulthood, show clear signs of senescent changes in older individuals.

Perhaps the most damaging evidence against the telomere clock theory comes from recent experiments in which genetically altered mice lost the telomerase enzyme that maintains telomere length. Six generations of mice with successively shorter telomeres still seemed to age at about the same rate as their normal ancestors.

**Clues from effects of caloric restriction**

While Miller doesn’t think that researchers have in any way found the aging clock, he feels that there are a number of very useful research paths that can give clues to how the clock operates. One path is to study the effects of caloric restriction and other dietary changes to try to find out the underlying biochemical changes that lead to life extension. “If we can find how caloric restriction works, what biochemical pathways are involved, we could eventually perhaps devise pharmacological methods of achieving the same results,” Miller comments.

There are hints of these mechanisms already. Caloric reduction produces low glucose levels in the blood, and aging researchers know that high glucose levels in the blood seem to accelerate several symptoms of aging. Another U-M researcher, Jeffrey B. Halter, M.D., director of the Geriatrics Center in the Medical School and medical director of the Institute of Gerontology, had studied the effects of obesity and lack of exercise, both of which raise blood glucose levels. “High blood sugar levels accelerate the damage to certain types of important molecules, somewhat akin to the browning of apples exposed to air,” he explains.

Other clues may come from studies that show that different kinds of nutritional reduction can also lengthen laboratory animal life spans. For example, Miller points out, recent research has shown that
just reducing the methionine (an essential amino acid) in rats’ diets extends their life span by 30 percent. Looking at common biochemical pathways that could be affected both by methionine reduction and caloric reduction, could lead researchers closer to the systems that determine the rate of aging. Additional experiments now underway on the effect of caloric reduction on rhesus monkeys could help to show how relevant this is to humans.

**Hunting the aging genes**

Another main research pathway is to try to find the genes that influence aging rates. Miller and his colleague David Burke, Ph.D., associate professor of human genetics and a senior associate research scientist in the Institute of Gerontology, have been exploring some of these areas. In one line of work, they are looking at mutations known to affect life spans in mice. For example, two dwarf mutations that produce mice about one-third the weight of normal mice also extend life span by 50-75 percent. Studying these mice may show how thyroid and pituitary hormones, deficient in the mutants, affect aging rates.

Such a link between growth and aging is also indicated by experiments in dietary restriction which result in impaired growth but longer life, although some lengthening of life span occurs even if these diets are started in full-grown animals.

“We’re also looking at wild mouse populations that we think are likely to be long-lived because of their more benign environments—those that have smaller, later litters,” Miller comments. Mapping genetic differences between naturally long-lived and normal strains can help map where aging genes lie. In another project, Burke and Miller are looking at what Burke calls “the world’s largest living family”: a group of 600 mice that are genetically equivalent to siblings. “We’re seeing how the life span, immune response, stress response and other markers for aging vary,” says Burke. “We think we will be able to narrow down genes that control some of these phenomena to perhaps a thousand genes or less than a tenth of a chromosome.

**Aging at the molecular level**

A third avenue of attack on the aging process is to determine what changes take place at the cellular and molecular levels. “We know that the DNA of cells doesn’t really change as the animal or human ages. But somehow the way genes express themselves as proteins changes, just as it does during development and differentiation—which we also don’t really understand,” says Burke. “The changes must be in the links between DNA and RNA or between RNA and proteins, and we are looking at how these changes occur in mice to try to find out.”

Ari Gafni, Ph.D., professor of biological chemistry and director and senior research scientist in the Institute of Gerontology, has been investigating one aspect of how proteins change with age. “We’ve found that proteins start to fold incorrectly in older cells and this can lead to diseases like Alzheimer’s,” Gafni explains. This seems to involve signals the cells get from the rest of the body. “We know that when liver cells regrow in an older mouse, initially the cells produce the good proteins, but within weeks they are producing the same wrongly folded proteins as other older cells.” Finding what those signals are may lead to another clue to how the aging process works and what controls it.
Over 800 patients, friends and supporters of Turner Geriatric Clinic attended the U-M Geriatrics Center’s celebration in recognition of the 1999 United Nations International Year of Older Persons last October at Rackham Auditorium.

The event featured a keynote address by Daniel Schorr, senior news analyst for National Public Radio, who began his career as a foreign correspondent in 1946, writing from postwar Europe for The Christian Science Monitor and later The New York Times. Schorr advised his audience, many of them, like him, in their 80s or older: “What you like to do, do. The people here could have chosen to retire. Instead they do things for other people. I’m being honored, but the honor is to me.”

Schorr received the U-M Geriatrics Center Outstanding Lifetime Achievement Award at a celebration that acknowledged the lifetime contributions of older adults and their vital role in community life.

Eight other community members received Turner Geriatric Clinic Community Lifetime Achievement Awards.

University of Michigan Music School faculty members William Bolcom and Joan Morris, the husband-and-wife performers noted nationally for their accomplished renditions of popular music from the 1920s and 1930s (he is a ragtime and jazz pianist and composer, she is a mezzo soprano cabaret singer) provided entertainment for the event. Their performance was in tribute to Katherine Morris, Joan’s mother and a former patient of Turner Geriatric Clinic. The celebration also served to mark the end of the first year of a campaign to raise funds for Turner Geriatric Clinic programs that benefit senior citizens and their families throughout southeastern Michigan.

Also participating in the program were Gilbert S. Omenn, executive vice president for medical affairs; Jeffrey B. Halter, director of the University of Michigan Geriatrics Center; and Ruth Campbell, the Geriatrics Center’s associate director of social work and community programs.

Charting the path ahead

Not all aging researchers by any means agree with Miller’s view of the field. In fact, even among U-M researchers, neither Burke nor Halter agree that there is probably a single, central aging clock, although Gafni does. Nor are all researchers focused on the general goal of finding such a clock and slowing it down. “I’m more interested in preventing premature aging and getting everyone up to 80 or 85 years, rather than extending the maximum human lifetime,” Burke states, and Halter concentrates on the prevention of the diseases of aging.

There is, however, a good deal of agreement that extending aging research could produce big benefits. “There are probably no more than 300 researchers worldwide working on the aging process,” Burke says. “The research is uncertain, funding is not abundant and the problems lie in the whole organism, not in a single limited specialty.” While billions are spent on specific diseases, research into the causes and control of aging receives no more than a few tens of millions, despite its huge potential for disease prevention. “If the publicity about telomeres spurs interest in the field, then it may be a boon,” says Miller. Given even a faint chance of slowing aging, he and his colleagues believe that a large expansion of effort could well be justified.
Graduate Student Welcome ’99

A Time to Meet, Greet and Honor as the Academic Year Begins

(Above) Anwar Dunbar and Scott Berger, both recruits to the first year of the Program in Biomedical Sciences, as are Dara Spearman and Allison Miller, pictured in the top photo.

(Right) Steven Goldstein, interim associate dean for research and graduate studies, presents an Outstanding Graduate Student Teaching Award to Karen Hinkle. Two such awards are made each year.

(Bottom Right) Dean Allen S. Lichter addresses students and faculty at the annual reception for graduate students held October 1, 1999 in the Hippocrates Court adjacent to the Taubman Library and Medical Sciences Research Building III.

(Bottom) Yu-chi Phen displays with pride her award for outstanding graduate student teaching accomplishments.

(Above) Rita Cowell, representing the Graduate Student Council of the Medical School, which organizes and sponsors the event, welcomes new and returning students to the academic year in Ann Arbor.
A Historic Convocation Becomes a Time for Heartfelt Thank Yous

Waiting for the convocation to begin: Allen S. Lichter, dean of the Medical School; Gilbert Omenn, U-M executive vice president for medical affairs and CEO of the Health System, talking with Harold T. Shapiro, eleventh U-M president and now president of Princeton University; Antonia Novello, U.S. surgeon general during the Bush administration and now health commissioner for the state of New York, talking with U-M President Lee C. Bollinger.
A
n afternoon convocation at Hill Auditorium on October 1 marked the beginning of the official celebration of the Medical School’s 150th anniversary. Dean Allen S. Lichter welcomed guests who had come to “pay homage to the 150-year legacy entrusted to us,” and noted the “fabulous tradition” of which they were all a part.

Nine speakers, each chosen to represent a particular time and personal vantage point in the School's contemporary history, talked about the influence of the School and medicine at Michigan on their lives.

Antonia Novello (Residency in Internal Medicine, 1974), former U.S. surgeon general and now health commissioner for the state of New York, expressed her gratitude for the School's “taking a chance on a kid from Puerto Rico” and for imbuing her with a sense of service, for never allowing her to “forget the people behind the statistics.”

Representing all the patients served by the University of Michigan Health system, 29-year-old Erik Morganroth described the 34 days he spent on cardiac life support and the 1995 heart transplant that saved his life.

Renowned neurosurgeon Keith Black (M.D. 1981, Residency in Neurosurgery 1987), director of the Maxine Dunitz Neurosurgical Institute at Cedars-Sinai Medical Center in Los Angeles, representing the 18,000 physicians who have received their M.D. degrees from the Medical School since 1851, described his 12 years at Michigan as “unequivocally the best years of my life; as a student, you always felt your education was the center of the faculty’s attention.”

William N. Hubbard, M.D., who served as dean from 1959 to 1970, noted wryly the program’s description of his tenure as “the golden era,” and said he thought rather it was the new century “that truly holds the promise of being the golden era.” All he had done, he said, was to “remove impediments to the potential of the faculty and students,” which he deemed to be the major responsibility of those, like him, whose role in the School’s history had been an administrative one.

“As a student, you always felt your education was the center of the faculty’s attention.”

—Keith Black
Former U-M President Harold T. Shapiro talked about his memories of the “courageous action on the part of many individuals” in the “high-stakes poker game” that was involved in raising $210 million to replace the 61-year-old “Old Main” Hospital with a new one in the 1980s, and the “forced march” of his own medical education that was part of the process. (Shapiro, now president of Princeton University, serves as head of the National Bioethics Advisory Commission.)

David Botstein (Ph.D. 1967), chair of the Department of Genetics at Stanford University School of Medicine, representing graduate students, expressed his thankfulness for the “blending of basic science and medicine” at Michigan, a blending, he said, that could have been accomplished only at Michigan where the “breadth of vision” far exceeded that found anywhere else at the time.

President Lee C. Bollinger and Gilbert S. Omenn, executive vice president for medical affairs, represented the current leadership of the University and the Health System. Both spoke of the revolution in the life sciences and its promise for the new century. Despite all we’ve learned over 150 years, Omenn said, “our ignorance is still a compelling challenge.”

Below: Third-year medical students Aaron Anderson, Neda Yousif, and Anita Lopes with their souvenir histories by Horace Davenport.

Right: Antonia Novello signs her autograph in first-year student Natalie Hubbard’s copy of the new Horace Davenport book, Not Just Any Medical School.


Left: Grateful patient Erik Morganroth, who received a heart transplant in 1995 at University Hospital.

Far Left: From left, on stage: Keith Black, William Hubbard, David Botstein, Allen Lichter, admiring the crystal memento given to each speaker.
“I’m thankful for the blending of basic science and medicine that could only have been accomplished at Michigan.”
—David Botstein

Top Left: Faculty members Jack Dixon and James C. Stanley (M.D. 1964, Residency 1970) leading the convocation processional down the aisle in Hill Auditorium.
Retired family physician Donald D. Finlayson (M.D. 1941), of Sault Ste. Marie, received the Lake Superior State University Distinguished Citizen Award in October, 1999. The award, which honors friends and advocates of Lake State, its students, faculty and staff, recognizes Finlayson’s many contributions to the school, including service as the University’s first school physician from 1946 until 1978. Furthering the honor, beginning in 2001 the award will be known as the Catherine and Donald Finlayson Award, named for the physician and his wife.

Paul Wolf (M.D. 1952) is professor of pathology at the University of California, San Diego. Earlier in his career he was professor of pathology at Stanford University, where he was director of clinical laboratories, and at Wayne State University in Detroit. He has received 10 consecutive Excellence in Teaching awards from the graduating fourth-year classes at the University of California Medical Center, and in 1997 he received the prestigious Albert Chaney Award from the California section of the American Association of Clinical Chemistry for his research and teaching related to clinical chemistry technology.

He can be reached by e-mail at paul.wolf@med.va.gov or by phone at (619) 552-8585, ext. 7762.

B. J. Woodley (M.D. 1956), a family physician practicing in Trenton and known for his pioneering surgical treatment of cardiac anomalies in infants and children, was selected as "Family Physician of the Year" by the Michigan Academy of Family Physicians. The Wayne County Medical Society’s Detroit Medical News announced Woodley’s award last fall, noting...
that he has long been “a keen observer of Michigan politics” who has been “instrumental in developing relationships between doctors and legislators, first locally in Wayne County and then later on the state level.” Woodley has been a member of the Wayne County Medical Society’s Legislative Committee since its inception in 1979.

1960s

Rogelio Pardo-Evans (Residency 1968) practices medicine and teaches at the Hospital San Juan de Dios in San Jose, Costa Rica, his native country. In 1998 he was appointed Minister of Health for Costa Rica and president of the Costa Rican Cancer Institute. He lives in San Jose with his wife, Susan Maurer, and their three children. He can be reached by e-mail at rpardo@pop.racsa.co.cr or by phone at (506) 235-2424.

1970s


1980s

Ronald L. VanderLaan (M.D. 1982) is the new president of the 1,000-member medical staff of Spectrum Health in Grand Rapids. He practiced with Grand Valley Cardiology Specialists from 1987 to 1999. He took his fellowship program in cardiovascular disease with the Cleveland Clinic Foundation and, before that, completed his internship and residency programs at Blodgett Memorial Medical Center (now Spectrum Health-East Campus) and Saint Mary’s Hospital in Grand Rapids. He was chief medical resident at Saint Mary’s in 1984. He is the immediate past president of the Michigan Society of Internal Medicine.

1990s

John A. Sandin (M.D. 1993) is in the chief year of his neurosurgery residency at the University of Wisconsin. He can be reached by e-mail at jsspines@yahoo.com or by phone at (608) 277-1099.

Todd B. Wampler (M.D. 1996) has received the F. William Barrows Award for Colorado Family Medicine Resident of the Year from the Colorado Academy of Family Physicians. He completed his residency in family medicine last fall at Poudre Valley Hospital in Fort Collins, Colorado. He is currently practicing at Buckley Air National Guard base in Aurora, Colorado, where he is fulfilling a military commitment. He lives in Fort Collins with his wife, Heidi, a student in veterinary medicine, and his daughters Kelcie, age nine, and Megan, age three. He can be reached by e-mail at twampler@pol.net or by phone at (970) 206-4550.

Your bequest to Michigan will help keep the Medical School great for another 150 years

A bequest is a wonderful way to ensure that the Medical School’s future will be as bright as its past. For some, a bequest offers the opportunity to make a more substantial gift than would be possible during a lifetime. For others, it’s an opportunity to round out many years of giving with a lasting legacy to the Medical School to meet faculty, student and program needs, and to enjoy the financial advantages associated with a bequest to a charitable institution. If you’d like to support the work of the School by establishing a bequest, please call the Office of Medical Development and Alumni Relations at (734) 998-7705. We’ll be happy to send you all the information you need to establish a bequest to advance medicine at Michigan.

If you would like information on other ways to make a gift, please call and request a copy of Ways of Giving to Advance Medicine at Michigan, which includes information on establishing a charitable remainder trust, establishing a lead trust, participating in the University’s Donor Pooled Income Fund, making a gift of cash, appreciated securities, real estate or personal property, or leaving retirement assets to advance medicine at Michigan.
Deaths

**George Ablin** (M.D. 1948), neurosurgeon, on June 8, 1999, in Bakersfield, California.

**John A. Jacquez**, M.D., on October 16, 1999, at University Hospital in Ann Arbor. Jacquez retired from the University of Michigan Medical School in 1990 as professor emeritus of physiology and from the School of Public Health as professor emeritus of biostatistics. A 1947 graduate of the Cornell Medical School, he came to Ann Arbor in 1962 from the Sloan Kettering Institute to establish a Department of Biomedical Data Processing, and was a leading authority on compartmental analysis. He was 77.

**Neil M. Kalter** (Ph.D. 1971), on October 23, 1999, at his home in Ann Arbor. A professor of psychology and psychiatry, he taught courses in advanced statistics, research methods, child psychotherapy, family therapy and parental loss. He was director of the University Center for the Child and Family from 1987-92. His work included the clinical supervision of psychiatry residents and fellows as well as trainees in psychology and social work. His contributions to the scientific literature included a wide array of journal articles and book chapters on topics including psychological tests, research methods and statistical analyses, children's understanding of their disturbed peers, and the impact of divorce and parent death on children. He was the author of *Growing Up with Divorce* (1990). He was 57.

**Carol Jo Godoshian Ragsdale** (M.D. 1972), on August 10, 1999, in Ann Arbor, of amyotrophic lateral sclerosis. She was an associate professor of pediatrics at the University of Michigan Medical School until 1993.

**A. Kenneth Stolpman** (M.D. 1931), on August 13, 1999, in Beverly Hills. A gynecologist and obstetrician, Stolpman practiced medicine in Birmingham for 55 years, starting in 1935. During World War II he served as a medical officer to the WAVES program at Indiana University and as a surgeon on the USS Arneb. He left the Navy with the rank of lieutenant commander. While at the University of Michigan, he earned a varsity letter in fencing. He was 91.

Stay in Touch

Share your news with those with whom you trained at the University of Michigan. Please send news (and photos or other art) to Jane Myers, 301 E. Liberty, Ann Arbor, MI 48104-2251; fax: 1-734-998-7268; e-mail: jemyers@umich.edu.

Please include your name, Michigan affiliation, current practice, titles, awards, postal address, telephone and e-mail address along with your professional and personal news.
Michigan’s Continuing Medical Education
Calendar Winter/Spring 2000

M A R C H
2-4  21st Annual Advances in the Management of Infectious Diseases: Winter Update
     South Seas Plantation, Captiva, Florida
7-10  Spring Family Practice 2000
      Towsley Center, Ann Arbor
25  Advanced Trauma Life Support (Refresher Course)
      Towsley Center, Ann Arbor

A P R I L
6-7  Innovative Medicine for Obstetrics and Gynecology
     Towsley Center, Ann Arbor
8  Common Problems in Office Practice
    Novi Hilton, Novi
14-15  Advanced Trauma Life Support (Instructor Course)
      Towsley Center, Ann Arbor
15  Transesophageal Echocardiography Seminar
    Sheraton Inn, Ann Arbor
17-19  Management of the Difficult Airway
      DoubleTree La Posada Resort, Scottsdale, Arizona

M A Y
4-6  28th Annual Spring Update in Internal Medicine
     Towsley Center, Ann Arbor
8-12  Practical Training in Vascular Interventions (featuring “Hands-on” Training)
     Animal Imaging Laboratory, Ann Arbor
12-13  Heart Failure and Cardiac Transplantation: Management into the Millennium
      Towsley Center, Ann Arbor
13  Oncology for Nurse Practitioners and Physician Assistants
    Towsley Center, Ann Arbor
19-20  Ophthalmology: Diagnosis and Management of Glaucoma
     Kellogg Eye Center, Ann Arbor
20  Office Management of Peripheral Vascular Disease
    Dearborn Inn, Dearborn Michigan
30  Automated Information Management in the Clinical Laboratory
    (Location to be determined.)

J U N E
2-3  Back Pain and Disability: Practical Solutions for Primary Care
     (Location to be determined.)
7-9  27th Annual Current Topics in Blood Banking
     Towsley Center, Ann Arbor
17  DDW (Digestive Disease Week) Wrap-Up
    Novi Hilton, Novi
19-23  35th Annual Northern Michigan Summer Conference
     Shanty Creek, Bellaire
22-24  First International Conference on Pediatric Continuous
     Renal Replacement Therapy (PCRT)
     Marriott Inn, Orlando, Florida
23-24  Advanced Trauma Life Support (Student Course)
     Towsley Center, Ann Arbor

Course dates may change. For verification or more information about course locations and
content, call or write: Office of Continuing Medical Education, Department of Medical
Education, University of Michigan Medical School, Box 1157, Ann Arbor, MI 48106-1157
Kathleen L. Collins, M.D., Ph.D., assistant professor of internal medicine and of microbiology and immunology, has been named a 1999 Pew Scholar in the Biomedical Sciences. Collins was one of only 20 Scholars chosen from nominations from over 100 institutions in the U.S. The Pew Charitable Trusts support non-profit activities in the areas of conservation and the environment, culture, education, health and human services, public policy and religion. Collins was selected for her promise as a biomedical researcher and will receive a total award of $240,000 to help support her research over a four-year period.

James M. Cooke, M.D., co-chief resident and house officer in the Department of Family Medicine, was selected to attend the 1999 C. Everett Koop Residency Physician Leadership Symposium. The Leadership Symposium is designed to promote resident leadership and was held in September, 1999.

James T. Elder, M.D., Ph.D., (Residency 1988) associate professor of dermatology and of radiation oncology, has been appointed to serve on the National Psoriasis Foundation’s (NPF) Medical Advisory Board. The NPF Medical Advisory Board counsels the NPF on technical and scientific matters and provides guidance in effective application of the organization’s resources in improving the medical treatment and control of psoriasis and psoriatic arthritis.
**TransWeb: A Web Site for Transplant Patients**

An early participant in the electronic media revolution, a 5-year-old U-M-based Web site dedicated to the concerns of transplant patients now receives more than one million visits a month. Entitled *TransWeb: All About Transplantation and Donation*, the site (www.transweb.org) provides reliable information about all aspects of transplantation. Users include transplant patients and their families, medical professionals, and teachers and students. *TransWeb’s* mission is to provide information about donation and transplantation to improve organ and tissue procurement efforts worldwide, to present information related to issues of concern to transplant patients and their families, and to provide an index of sources for transplant-related information. In September of 1999, *Popular Science* ranked the *TransWeb* site one of the five best sites on health and medicine in the world. Pictured above: *TransWeb* Editor Eleanor Jones (center) and the *TransWeb* Editorial Board, from left to right, Jeffrey Punch, M.D., assistant professor of surgery; Jim Dean, senior programmer analyst; Robert Garypie, organ preservation specialist; Robert Merion, M.D., associate professor of surgery; and Alan Leichtman, M.D., associate professor of internal medicine.

**David Engelke**, Ph.D., professor of biological chemistry and director of the Program in Biomedical Sciences (PIBS), has been chosen by the U.S. Department of Health and Human Services to serve as chairperson of the Cell Development and Function Study Section, Center for Scientific Review. According to the NIH, “the skill and leadership offered by the chairperson determine to a significant extent the effectiveness and efficiency of the review group.” Engelke will serve as chair through June 30, 2001.

**A. Oveta Fuller**, Ph.D., associate professor of microbiology and immunology, and **Denise Kirschner**, Ph.D., assistant professor of microbiology and immunology, have been chosen to receive Career Development Awards by the Michigan Agenda for Women. This is an award established to acknowledge contributions to the University by female faculty members. The discretionary funds ($5,000) can be used for books, travel for professional activities, graduate student support or other purposes. The funds were established under the Michigan Agenda for Women and through the Office of the Vice President for Research.
Jameelah Gater, a fourth-year student in the Medical School, was elected student delegate to the American Academy of Family Physicians Congress of Delegates. The AAFP Congress is composed of two physician delegates from each of the 50 states and U.S. territories as well as two national representatives from the following constituencies: new physicians, women, uniformed services, residents, and students. Representing the student voice for the nation, Gater testified and voted on health care issues at the annual congressional meeting in Florida in September, 1999. This new position also allows Gater to function as a member of the National Committee on Resident and Student Affairs (CRSA) which deals with issues ranging from licensure to cultural diversity awareness and competency. She is also active at the state level currently serving on the Michigan Academy of Family Practice Board of Directors, CRSA, and Statewide Student Day Planning Committee.

Janet Gilsdorf, M.D., professor of pediatrics and communicable diseases, received the third annual 1999 Journal of General Internal Medicine Creative Writing Award for Prose for her short story, “Off to the Left.” Gilsdorf’s work was chosen from more than 70 submissions and was published in the June 1999 issue (Vol. 14, No. 6). The Journal of General Internal Medicine is the official journal of the Society of General Internal Medicine.

Susan Dorr Goold (M.D. 1987, Fellow 1992), assistant professor of internal medicine, has received a four-year grant from the Robert Wood Johnson Foundation for her research project “Consumer Values and Preferences in Managed Care.” The Robert Wood Johnson Foundation is the largest philanthropy organization devoted exclusively to health and health care.

Carmen R. Green, M.D., assistant professor of anesthesiology and director of the Acute Pain Service, was named the Woman of the Year in Human Relations by the University of Michigan’s Women of Color Task Force.

In nominating Green for the award, Kevin Tremper, M.D., Ph.D., chair of the Department of Anesthesiology, noted that Green “has been a role model for women of color and women in medicine” and praised her work in training nurses in acute pain management, in directing the clinical experience and clinical research experience for medical students in the summer between their first and second years, and in coordinating the Midwestern Anesthesia Residents Conference.

Lazar J. Greenfield, M.D., Frederick A. Coller Distinguished Professor and chair of surgery, has been elected secretary general of the International Society for Cardiovascular Surgery. The mission of the Society is to provide an international forum for the presentation, discussion, and dissemination of the state of the art and science of cardiovascular disease and its treatment to those professionals.

Peter Hedera, M.D. (Neurology Residency 1998), house officer in medical genetics in the Department of Pediatrics and Communicable Diseases, has received the Founders Award of the Auxiliary of the American Academy of Neurology. This award is designed to encourage clinical research in neuroscience by physicians in clinical neurology training programs. Hedera received this award for his genetic research on hereditary spastic paraplegia.

Robert B. Kiningham, M.D. (Residency 1992, Fellow 1993), clinical assistant professor of family medicine and director of the Primary Care Sports Medicine Fellowship, was named a fellow of the American College of Sports Medicine. The American College of Sports Medicine promotes and integrates scientific research, education, and practical applications of sports medicine and exercise science to maintain and enhance physical performance, fitness, health and quality of life.

Michael S. Klinkman (M.D. 1982, Residency 1985), associate professor of family medicine, received the 1998 Volunteer Physician of the Year award from the Hope Medical Clinic in Ypsilanti.

The Hope Medical Clinic is a non-denominational Christian medical outreach clinic that provides free medical and dental care to all those with unmet health care needs and no access to care. It has served thousands of persons in need during the past 15 years.

Arno K. Kumagai, M.D., assistant professor of internal medicine, was recently recognized as one of only 44 physicians nationwide selected by medical students for the 1999 Association of American Medical Colleges’ Humanism in Medicine Award. Kumagai was nominated by the AAMC Organization of Student Representatives as a physician embodying the finest qualities in a healer who teaches healing. The nomination stated that Kumagai “demonstrates an unusual compassion and understanding of people and quickly puts people at ease... he was always sensitive to patients’ needs and went out of his way to provide the highest quality of care. It is no wonder that Dr. Kumagai has a very loyal following of patients who often insist on seeing only him as their diabetes health care specialist.”

Ralph Lydic, Ph.D., Bert La Du Professor of Anesthesiology, associate chair for anesthesia research and professor of physiology, has been elected the 1999 president-elect of the U.S. Sleep Research Society. The Sleep Research Society’s mission is to promote understanding of the processes of sleep and its disorders through research, the training of practitioners of research, and the dissemination of their research results to the scientific and medical communities as well as the general public.

continued
Lydic’s research ranges from transmembrane cell signaling to integrative aspects of respiratory and arousal state control. These studies aim to elucidate the cellular and molecular mechanisms that cause respiratory depression during the loss of waking consciousness. Lydic’s studies are funded by the National Heart, Lung, and Blood Institute because of their potential clinical relevance to disorders such as sudden infant death syndrome, adult sleep apnea, and anesthesia-induced respiratory depression.

The December 9, 1999, issue of the Wall Street Journal featured a commentary in the Leisure & Arts section by Howard Markel, M.D., associate professor of pediatrics and communicable diseases and director of the Historical Center for the Health Sciences, and Ada Louise Huxtable. Entitled “Ghosts of Hope and Despair: Ellis Island’s Abandoned Hospitals Are Crumbling Reminders of America’s Immigrant Story,” the column was an urgent plea to save the abandoned hospital buildings on Ellis Island, closed for almost 50 years now, that tell their own story of immigrant hope and despair. Markel and Huxtable are both among the first group of fellows selected to do scholarly work for a year at the Center for Scholars and Writers at the New York Public Library. Huxtable is a noted architecture critic.

Harold Oberman, M.D. (Internship 1957, Residency 1961), professor of pathology and director of the Blood Bank and Transfusion Service, was given the Founders Award of the Michigan Association of Blood Banks at its annual meeting on September 16, 1999.
Deborah C. Otteson, a graduate student in the program for cell and developmental biology working in the lab of Peter Hitchcock, Ph.D., associate professor of ophthalmology and visual sciences and of anatomy and cell biology, received the Chapter Award from the Michigan Chapter for the Society of Neurosciences for 1999 for her work, "Expression patterns of IGF-I and IGF-I receptor mRNA suggest an autocrine/paracrine role for IGF during retinal growth and regeneration in goldfish." Otteson presented her research at the Society’s annual meeting held at the Fetzer Center of Western Michigan University in May.

Otteson successfully defended her thesis, “Morphogenesis, Neurogenesis and Regeneration in the Retina: Genetic, Cellular and Molecular Biological Perspectives,” in December, 1999. She will be doing post-doctoral research at the Wilmer Ophthalmological Institute at the Johns Hopkins University School of Medicine in the laboratory of Donald Zack, M.D., Ph.D., as a post-doctoral fellow on the Visual Neuroscience Training Program.

James Peggs, M.D., clinical associate professor and senior associate chair in the Department of Family Medicine, has been selected by the Michigan Academy of Family Physicians as 1999 Family Practice Educator of the Year.

Mack T. Ruffin IV, M.D., M.P.H., associate professor of family medicine, received the 1999 Outstanding Medical Alumnus Award from the Medical College of Virginia.

David Ginsburg, Julian Hoff and Michael Marletta Named to the National Academy of Sciences’ Institute of Medicine

Three noted researchers from the Medical School have been named to the National Academy of Sciences’ Institute of Medicine. David Ginsburg, M.D., Julian T. Hoff, M.D., and Michael A. Marletta, Ph.D., were among 55 new members in the U.S. named in 1999. They join approximately 20 U-M faculty, current and former, named to the 588-member body.

Election to the Institute of Medicine, the medical arm of the National Academy of Sciences, is an honor reserved for those who have made major contributions to health and medicine or related fields. One-fourth of the members are drawn from outside the traditional health professions. Members volunteer their time on committees devoted to studies on a broad range of health policy issues.

David Ginsburg, M.D., holds joint appointments in the U-M Medical School’s Departments of Internal Medicine and Human Genetics as the Warner-Lambert/Parke Davis Professor of Medicine, chief of the Division of Molecular Medicine and Genetics and professor of human genetics. He is also an investigator of the Howard Hughes Medical Institute.

Ginsburg has been cited as a leader in the effort to find the molecular genetic basis of human bleeding and clotting disorders. Notably, he has focused on the von Willebrand factor, or VWF, a protein central to the body’s blood coagulation system. About one percent of the general population may have an inherited bleeding disorder caused by abnormal VWF. Ginsburg’s work began with the cloning of the von Willebrand factor gene and now includes studies of how mutations in this gene lead to bleeding, and how mutations in other genes may also regulate VWF levels in the blood.

Ginsburg and his team also research how blood clots are dissolved, and how abnormalities in this process contribute to human diseases including heart attack and stroke. Most recently, his studies identifying the cause of another inherited bleeding condition have revealed important new information about how many proteins, including clotting factors, are transported within and out of cells.

Julian Hoff, M.D., is head of the Neurosurgery Section and professor in the U-M Medical School Department of Surgery. He also heads the Neurosurgery Training Program, one of the most sought-after neurosurgery residencies in the nation.

Julian Hoff: A "triple threat" neurosurgery educator who combines clinical practice, teaching, and research in a way that has brought him to national prominence and enabled him to influence the future of surgery.

Julian T. Hoff, M.D.

Michael Marletta: His work on determining the biochemical precursor to nitrates and nitrates led to the discovery of a previously unknown metabolic pathway.

Michael Marletta

David Ginsburg: A leader in the effort to find the molecular genetic basis of human bleeding and clotting disorders.

David Ginsburg, M.D.
His Institute of Medicine nomination called Hoff a “triple threat” neurosurgery educator who combines clinical practice, teaching and research in a way that has brought him to national prominence and enabled him to influence the future of surgery. A clinical specialist in acoustic tumors, cervical spine surgery and brain tumors, Hoff has also conducted laboratory research on cerebral edema and intracerebral hemorrhage funded by the National Institutes of Health for 25 years. He has received two NIH neuroscience awards.

His leadership activities in neurosurgery education include terms on the Residency Review Committee for Neurosurgery, as chairman of the American Board of Neurological Surgery, and as chair of task forces on neurosurgery resident education and fellowship. A past president of the American Association of Neurological Surgeons and of the American Academy of Neurological Surgeons, he is now president-elect of the Society of Neurological Surgeons, the principal society for neurosurgery educators, and second vice president of the American College of Surgeons.

Michael A. Marletta, Ph.D., is the John G. Searle Professor of Medicinal Chemistry in the U-M College of Pharmacy and a professor of biological chemistry in the U-M Medical School, as well as a Howard Hughes Medical Institute investigator. He also serves as chair of the Biological Sciences Scholars Program in the Medical School.

Marletta’s initial basic research on the biochemistry of nitrogen-containing compounds in the body has led to important knowledge about how cells send signals to one another, and has additional implications in toxicology. Specifically, his work on determining the biochemical precursor to nitrates and nitrites led to the discovery of a previously unknown metabolic pathway that produced the potent toxin nitrous oxide, or NO. These novel findings provided the basis for other researchers’ work on NO and Marletta’s analysis of the enzyme and chemical mechanism that result in NO formation in humans and other animals. His work was featured in the Spring 1999 issue of Medicine at Michigan.

Nitrous oxide is now known to be an important signaling molecule in the body, but it was a mysterious one until Marletta and his colleagues solved the riddle of how it can send signals from one cell to another when its chemical reactivity with oxygen should cause it to decompose rapidly, preventing its function as a signaling agent. Further, his studies have shown how NO is able to signal without killing the cells that produce it. His work on the cellular receptor that captures NO molecules and keeps them from reacting with oxygen is important to the ongoing understanding of NO’s role in intercellular communication. These basic science discoveries have now led to NO’s being used clinically to treat pulmonary hypertension, and have suggested treatments for stroke, colitis and toxic shock syndrome.
Following is a complete listing of all faculty and students who received awards at the 1999 Honors Convocation.

**FACULTY AWARDS**

**American Medical Women’s Association Gender Equity Award**
Elizabeth M. Petty, M.D.
Assistant Professor of Internal Medicine
Assistant Professor of Human Genetics

**Elizabeth Crosby Award**
Joseph M. Metzger, Ph.D.
Associate Professor of Physiology
Associate Professor of Internal Medicine

**Healthcare Foundation of New Jersey Humanism in Medicine Award**
Arno K. Kumagai, M.D.
Assistant Professor of Internal Medicine

**Kaiser-Permanente Awards for Excellence in Teaching**
Michael D. Jibson, M.D., Ph.D.
Clinical Assistant Professor of Psychiatry
Mel L. Barclay, M.D.
Associate Professor of Obstetrics and Gynecology

**DEPARTMENTAL AWARDS**

**Association for Academic Surgery Student Research Awards**
Patrick J. Javid
Keith G. Wolter

**Albert M. Barrett Award**
Katherine E. Mulder

**Roger A. Berg Prize in Radiology**
Dorothy M. Pao

**C. Gardner Child III Award**
Patrick J. Javid

**1999 Honors Convocation Awardees**

**Terence C. Davies Award**
Lisa M. Long

**Excellence in Emergency Medicine Award**
Rosemarie Fernandez

**Albert C. Furstenberg Award**
Christopher D. Lansford

**Edgar A. Kahn Award**
Vishal C. Gala

**William Dodd Robinson Award**
Michael E. Widlansky

**Eli G. Rochelson Memorial Award**
Seema Baranwal

**Robert B. Sweet Award**
Eric Huang

**William B. Taylor Dermatology Award**
Jason B. Van Ittersum

**Harry A. Towsley Award**
Amy P. Benzing

**Raymond W. Waggoner Award**
Tracey S. Oppenheim

**Carl V. Weller Award**
Neda N. Yousif

**J. Robert Willson Award**
Jennifer A. Zelenock

**SENIOR AWARDS**

**Dean’s Awards for Research Excellence**
Arul M. Chinnaiyan
Rosemarie Fernandez

**George R. DeMuth Medical Scientist Award for Excellence**
David P. Olson

**Ralph M. Gibson Award**
Tiwanda C. Williamson

**Healthcare Foundation of New Jersey Humanism in Medicine Award**
Matthew M. Bressie
James Neel, Father of the Field of Human Genetics, Dies at 84

James Van Gundia Neel, M.D., Ph.D., professor emeritus of human genetics and internal medicine at the University of Michigan, died of cancer February 1 at his home in Ann Arbor. He was 84 years old. An internationally renowned scientist, Neel was a pioneer in the study of human genetics and one of the first to foresee its importance in the diagnosis and treatment of medical conditions. During his 39-year career in the U-M Medical School, Neel established one of the first clinics to evaluate and counsel people with hereditary diseases, as well as the first academic department of human genetics in the United States.

Neel was the first scientist to recognize the genetic basis for sickle cell anemia. He conducted an extensive study on the aftereffects of atomic radiation on survivors of Hiroshima and Nagasaki and their children. During the 1960s, he proposed the “thrifty gene” hypothesis, which states that genes associated with common modern diseases like diabetes, hypertension and obesity are part of the human gene pool, because they helped our early ancestors survive when calories and salt were less abundant. Neel also was widely known for his studies of the genetic consequences of consanguineous marriage, the timing of human migration into North America and the genetic characteristics of isolated tribes in the Amazon rain forest.

His 39-year career in the Medical School was one of great vision and achievement.

Neel’s most recent research focused on severe chromosomal damage in what he named “rogue cells,” which he first identified in his studies of the Yanomama tribe in the Amazon and Japanese populations. Neel suggested that the origins of this chromosomal damage could be attributed to infection with human Polyomaviruses.

"Jim Neel was one of the most distinguished faculty in the 150-year history of this medical school," said Allen S. Lichter, M.D., dean of the U-M Medical School. "He was a true visionary in how genetics would one day be used, not only to determine the cause of disease, but also to treat it. He trained some of the finest minds in the field and his international reputation was impeccable."

"Dr. Neel was the father of the field of human genetics. He was the first to introduce a long list of bedrock principles, which we now take for granted," said Francis S. Collins, M.D., Ph.D., director of the National Human Genome Research Institute, who is on leave from the U-M Medical School. "He made a habit of being ahead of his time. Today, the Human Genome Project and associated advances in genetics are making it possible to test many of his hypotheses. There are growing signs that he was right on target.”

Neel was born on March 22, 1915, in Hamilton, Ohio, and received his A.B. degree in 1935 from the College of Wooster in Wooster, Ohio. After receiving his Ph.D. (1939) and M.D. (1944) from the University of Rochester, he completed his internship and residency at the Strong Memorial and Rochester Municipal Hospitals.

Neel joined the U-M faculty in 1946 as an assistant geneticist in the Laboratory of Vertebrate Biology. From late 1946 to 1947, he served in the Army Medical Corps and directed field studies for the Atomic Bomb Casualty Commission of the National Research Council. In 1948, he returned to the U-M to direct the Institute of Human Biology Heredity Clinic. Neel established the U-M Medical School’s Department of Human Genetics in 1956, which he chaired for 25 years. He was named the Lee R. Dice University Professor of Human Genetics in 1966—a position he held until his retirement on June 30, 1985.

"Jim Neel’s contribution to the studies of populations throughout the world and in patients right here in Michigan are seminal and legendary," said Gilbert S. Omenn, M.D., Ph.D., U-M executive vice president for medical affairs. "He has been one of our most prominent faculty members and a great presence on this campus for more than five decades. He was completing additional collaborative research up to the time of his death, with work that will continue for several years."

"Not only was James Neel a pioneer in human and medical genetics, he always kept foremost the physician’s perspective," said Thomas D. Gelehrter, M.D., professor and chair of the U-M Medical School’s Department of Human Genetics. "He had a keen sensitivity to the societal implications of the knowledge he discovered. He truly embodied the title of his remarkable book, ‘Physician to the Gene Pool.’"

Memorial contributions can be made to the James V. Neel Fund at the U-M, which will be used to support an annual fellowship and an annual lectureship in the Department of Human Genetics. Contributions should be sent to: Medical Development and Alumni Relations Office, 301 E. Liberty, Suite 300, Ann Arbor, MI 48104-2251. —Sally Pobojewski
The newest class of students in the University of Michigan Medical School donned their first-ever white clinician’s coats and affirmed “that into whatsoever house I shall enter, it shall be for the good of the sick to the utmost of my power” and the several other solemn promises of the Hippocratic oath in the fourth annual White Coat Ceremony on the stage of Rackham Auditorium in mid-August.

A growing number of medical schools, including the University of Michigan Medical School, have begun welcoming new students with the white coat ceremony to honor the beginning of their medical training and eventual careers in medicine, with special emphasis on the importance of empathy and caring in the doctor-patient relationship.

“The White Coat Ceremony is a way of highlighting the sense of professionalism inherent in the practice of medicine,” said Gerald D. Abrams, M.D., professor of pathology, who delivered the day’s keynote address, “The Journey Begins.” “The ceremony emphasizes to students, at the outset of their training, the moral obligation to achieve technical excellence, to gain a compassionate understanding of the human dimensions of illness, and to become fully dedicated to the care of their patients.

“It is also a means of demonstrating our commitment, as faculty, to helping them in every way to become full-fledged members of a profession with a proud tradition. Finally, the ceremony provides a wonderful opportunity for the students’ families and friends to share the joy of their entry into the profession.”

Arnold Gold, a professor of clinical neurology and clinical pediatrics at Columbia University’s College of Physicians and Surgeons for the past 40 years, has been a strong advocate for the white coat ceremony at medical schools across the country since 1993, as has the Robert Wood Johnson Foundation. The ceremony at Michigan is currently supported by the Medical School and the Medical Center Alumni Society.
Top Left: Layne Kumetz (center) of Los Angeles, California, gets her picture taken by mother Robbie Kumetz with West Bloomfield cousins Nancy Tuttleman, Carolyn Jacobs, Lesley Jacobs, and Pam Freed.
Top Right: Hien Duong, from Whitehall, with her congratulatory bouquet of red roses.
Center Left: Carla Newcomb removes wrinkles from son David Newcomb’s white coat for his first-ever photo in his clinician’s garb as wife Kelly looks on. Newcomb is from Sanford.
Center Middle: Ann Arborite Alice Lin, recipient of a scholarship this year from the Norman H. Mette Foundation.
Center Right: Gerald D. Abrams, M.D., professor of pathology, delivers the keynote address, ‘The Journey Begins.’
Bottom Left: Natalie Hubbard of Detroit prepares to be cloaked by Dean Lichter.
Bottom Right: Dean Lichter helps Ian Mutchnick on with his white coat on the stage of Rackham Auditorium. Mutchnick is from Saline.
JAMA Honors Medicine at Michigan
Eight articles by U-M authors featured

The February 16, 2000, issue of the Journal of the American Medical Association, which celebrates the University of Michigan Medical School Sesquicentennial, contains eight articles including original research, essays, and editorial commentary authored or co-authored by Michigan faculty. Listed in the approximate order in which they appear in the Journal, they are:

♦ Indications for Emergent Magnetic Resonance Imaging of the Brain and Spine by Douglas J. Quint, M.D.

A discussion of the appropriateness of magnetic resonance imaging for evaluation of suspected central nervous system pathology on an emergent basis, and clinical situations, such as suspected spinal cord compression, when emergent magnetic resonance evaluation is required.

♦ A Cost-Utility Analysis of Screening Intervals for Retinopathy in Type 2 Diabetes by Sandeep Vijan, M.D., Timothy P. Hofer, M.D., and Rodney A. Hayward, M.D.

An examination of the marginal cost effectiveness of various screening intervals for eye disease in type 2 diabetes, stratified by age and level of glycemic control.

♦ The International Registry of Acute Aortic Dissection: New Insights into an Old Disease by Kim Eagle, M.D., and many other authors of a large international study

An assessment of the presentation, management and outcomes of acute aortic dissection, a life threatening emergency associated with high morbidity and mortality, based on outcomes of 464 patients over three years.

♦ Extracorporeal Life Support: The University of Michigan Experience by Robert H. Bartlett, M.D., Dietrich W. Roloff, M.D., Joseph R. Custer, M.D., John G. Younger, M.D., and Ronald B. Hirschl, M.D.

A description of the Michigan experience, over two decades, with extracorporeal life support (the use of a modified heart-lung machine) with 1,000 patients, the development and current status of extracorporeal life support, and diffusion of this complex technology into clinical practice.

♦ Conflicts around Decisions to Limit Treatment: A Differential Diagnosis by Susan Dorr Goold, M.D., Brent Williams, M.D., M.P.H., and Robert M. Arnold, M.D.

A medical model proposed as a useful tool for helping physicians to understand and manage physician-family conflicts about end-of-life care.

♦ An Example Worthy of Imitation: The University of Michigan Medical School, 1850-2000 by Howard Markel, M.D., Ph.D.

A brief history of the Medical School, its vital reforms in medical education, and its success as a public institution of higher learning charged with educating students of diverse backgrounds.

♦ ERISA Litigation and Physician Autonomy by Peter D. Jacobson, J.D., M.P.H., and Scott D. Pomfret, J.D.

A look at the Employee Retirement Income Security Act, how the complex statute influences health care delivery in managed care organizations, and how court interpretations of ERISA have limited physician autonomy and subordinated clinical decision-making to managed care organizations’ cost-containment considerations.


An overview of challenges faced and met by the U-M Health System as an academic medical center in the late 1990s, and its ongoing commitment to integrating medical practice with education and research.

In addition to the above articles, five books authored or co-edited by Michigan faculty will be reviewed in the JAMA issue celebrating the Medical School Sesquicentennial. They are as follows:


The Practice of Autonomy: Patients, Doctors, and Medical Decisions by Carl E. Schneider, J.D. Reviewed by George J. Annas, J.D., M.P.H., of the Health Law Department at the Boston University School of Public Health.


Sleep Medicine by Michael S. Aldrich, M.D. Reviewed by Randolph W. Evans, M.D., Houston, Texas.

From the University of Michigan Health System: Executive Officers (Omenn, Lichter, and Warren), Departments of Radiology (Lichter, Quint), Internal Medicine (Vijan, Hofer, Hayward, Eagle, Goold, Williams, Halter, Schneider, Yamada, Owyang, Omenn), Surgery (Bartlett, Hirschl), Pediatrics and Communicable Diseases (Roloff, Custer, Markel), Emergency Medicine (Younger), Physiology (Davenport, Yamada), Neurology (Aldrich), Human Genetics (Omenn), Geriatrics (Halter), Historical Center for the Health Sciences (Markel). Also: School of Public Health (Jacobson, Hayward), Law School (Schneider), Office of the U-M President (Bollinger).

Medical School alumnus Michael E. Johns (M.D. 69, Residency in Otolaryngology 1975) is executive vice president for health affairs at Emory University in Atlanta, Georgia.
I want to share with you the following commentary, which I co-authored with Dean Allen Lichter, Hospitals Executive Director Larry Warren, and U-M President Lee Bollinger. This article appears in the February 16, 2000, issue of the Journal of the American Medical Association. Entitled “Shaping a Positive Future for Academic Medicine at Michigan,” it highlights challenges we have faced and met as an academic health system, including important new initiatives in the Medical School. It is one of seven peer-reviewed original articles to appear in the issue by U-M Medical School authors, along with a wonderful historical piece by Howard Markel, who organized the special issue.

The University of Michigan (U of M) is proud to celebrate a splendid legacy of innovation and service at the 150th anniversary of its medical school. Some notable achievements in our history include the establishment of the first university-owned teaching hospital in 1869, enrollment of women and African American medical students in the 1870s, development of iodized table salt as a goiter preventive, early advances in electrocardiography, the first thoracic surgery section and introduction of thoracoplasty for tuberculosis, the development and progressive application of extracorporeal life support, discovery of the gene for cystic fibrosis, investigation of gene therapies for cardiovascular diseases and muscular dystrophies, and new forms of managed care. However, we cannot rest on our laurels.

Instead of considering our academic mission a costly burden on patient care, we reaffirmed our commitment to integrating medical practice with education and research. At a time of spectacular research breakthroughs in the life sciences and advances in medical care, all academic medical centers face serious financial stress due to employers’ and governments’ determination to control health care spending. Negatives stereotypes are widespread among patients, payers, employers, referring physicians, and the media, who tend to describe university-affiliated medical centers and medical schools as aloof from their communities, too expensive, biased toward patients with less common diseases, and slow to change.

Our wake-up call came in 1996. Under pressure from employers and payers to reduce cost per case and facing a modest operating deficit, the hospital leadership stepped up quality improvement programs while eliminating 1050 positions and laying off 200 employees. Conflicts between the hospital director and medical school dean about priorities, a gloomy outlook about NIH research funding, and insufficient sites for ambulatory teaching inspired new leaders of the medical school and the hospital to align more explicitly strategic, operational, and financial objectives of the faculty and the hospitals. A unified faculty group practice emerged from the “silos” of 15 department-based practices. The group practice, hospitals, and health centers were united in a clinical delivery system that would stimulate patient care and academic collaborations across departments and ensure joint attention to the overall bottom line.

Instead of considering our academic mission a costly burden on patient care, we reaffirmed our commitment to integrating medical practice with education and research. In 1997, the medical center was renamed the University of Michigan Health System to highlight the geographic reach of 32 ambulatory health care centers, various strategic affiliations, and the central role of the medical school. Through grant-supported programs to train residents in managed care and through overall system investments in medical management, disease management, and pharmacy practices, we are also gaining synergies from our own health maintenance organization, the 190,000-member M-CARE health plan. Proposals for separating the hospital from the rest of the university and for mergers with other provider systems were rejected at the U of M; it was our belief that such actions would undermine our academic mission, force the integration of different provider cultures, and create a situation of incompatible governance. Attention was focused instead on better service to patients and to referring physicians; credible measures of patient satisfaction, productivity, quality, and cost-competitiveness; instructional innovations; and an improved research infrastructure. We have seen a growth in clinical volumes with positive operating margins.

In concert with the organizational changes, we have made a sustained effort to change the culture. The hospitals and health centers adopted the theme “Putting Patients and Families First.” Under this banner, professionals and support staff were brought together with common goals; many commented that service to patients was their initial motivation for pursuing a career in health care. Essentially, the theme reflects the approach of
asking all staff to imagine themselves or their family members as the patients. Our progress in this regard has been quantified and benchmarked through participation in surveys of patients’ perceptions of care throughout southeast Michigan. Gain-sharing programs were tied to improved satisfaction scores. Concerns about timely communication, expressed by a committee of referring physicians, were addressed by providing physicians with toll-free telephone, facsimile, and e-mail communication opportunities to keep them informed about treatment plans and necessary follow-up, all accomplished in real time. We are trying to look at ourselves as others see us.

We are trying to look at ourselves as others see us.

Although control of costs remains challenging, we have reduced cost per case 20% through clinical unit redesign, volume purchasing, and spreading fixed costs over increased inpatient admissions and outpatient visits. We have sought innovative ways to control costs. For example, the General Motors “PICOS” (a Spanish term for peaks of mountains) team of system engineers helped us assess operating room and postoperative procedures: average cardiac surgery duration of about 5 hours was reduced by 72 minutes. Consultants from the Ritz-Carlton Hotel Company guided the department of dermatology with suggestions to improve customer service, empower staff, and improve patient flow, resulting in increased patient satisfaction and decreased staff turnover. For fiscal year 2000, every hospital and ambulatory unit is accountable for 4% downward “rebasing” of budgets, adjusted for volumes.

A special test of our capacity for change occurred in late 1997, when the Ford Motor Company challenged the U of M to develop a proposal for a new health care plan with the company. Physicians, hospital administrators, and M-CARE staff were given 5 working days to prepare a presentation; four days after the proposal was submitted, Ford announced Michigan as its partner. The company knew that 18% of its workforce accounted for 86% of its health care costs and wanted to cooperatively design a disease management program. After months of analysis and negotiation, the plan called “Partnership Health” emerged. This plan features systematic disease management for all enrollees in 5 initial diagnostic categories (congestive heart failure, coronary artery disease, asthma, diabetes, depression); a key role for patient advocates called “health navigators”; and opportunities for enrollees to name their own personal physicians, who are accepted into the University of Michigan Health System/Ford Partnership Health network if they agree to practice under Partnership Health guidelines. The plan is exceeding expectations. It is certain that the pace of change in medicine will accelerate in the years leading toward our bicentennial. Institutions that can respond to those changes while remaining focused on service, productivity, and market leadership will shape a positive future for academic medicine.

Meanwhile, the health system and the medical school have increased investments on the academic side. We have combined the recruitment, admissions, curricular, and mentoring aspects of 6 departmental and 5 interschool doctoral programs into a comprehensive program in biomedical sciences. We have launched a Center for Clinical Investigation and Therapeutics to make designing and conduct of clinical research more efficient for busy clinical investigators. The center provides support in biostatistics, a patient registry, nurse coordinator and physician training, guidance in meeting institutional review board compliance requirements, and expertise in quality of life and pharmaeco- economics assessment. We have tripled our $5 million investment in bioinformatics with foundation and corporate funding. We have created internal funds to support combined clinical and basic research proposals and for proof-of-concept studies of new technologies. We have 3 cohorts of 12 faculty members, each selected as “educational innovators,” for a year-long program developing and implementing teaching modalities for biomedical advances, changes in medical practice, and meeting the needs of a multicultural society.

Following a special U of M Presidential Commission report, the university has committed $200 million for a Life Sciences Institute; major involvement of the health system in this investment reflects confidence that advances in genetics, structural biology, cognitive neurosciences, bioinformatics, and biomedical engineering will transform medical care and enhance the health system’s clinical competitiveness in concert with the academic mission. In parallel, the state has initiated a $50 million per year, 20-year commitment for a collaborative Life Sciences Corridor among Michigan’s research institutions and companies.

It is certain that the pace of change in medicine will accelerate in the years leading toward our bicentennial. Institutions that can respond to those changes while remaining focused on service, productivity, and market leadership will shape a positive future for academic medicine.

Gilbert S. Omenn, M.D., Ph.D.
U-M Executive Vice President for Medical Affairs and CEO, U-M Health System


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