

# THE NIH RECORD

Still The Second Best Thing About Payday

*National Medal of Science Winner*

## Wilson To Give NIH Director's Lecture, Sept. 11

By Joanna Mayo

"The Future of Life," is the topic of the NIH Director's Lecture that will be given by the internationally acclaimed entomologist and biological theorist Dr. Edward O. Wilson on Wednesday, Sept. 11 at 3 p.m. in Masur Auditorium, Bldg. 10.

Wilson is the Pelligrino university research professor emeritus at Harvard University, honorary curator in entomology at the Harvard Museum of Comparative Zoology, and a Pulitzer Prize-winning author. His most recent book, *The Future of Life* (2002), describes a biologically complex world that has been negatively affected by human activity. Two decades of research on biological diversity has led to his prediction that one-half of the Earth's species is in danger of disappearing by the end of this

SEE WILSON, PAGE 2

## EHRP System To Debut Sept. 9

Last February, the *NIH Record* informed NIH'ers about the new arm of a major unseen construction project on campus. The project is an administrative undertaking known as the NIH Business and Research Support System, and its extension is the new automated personnel system, the Enterprise Human Resources and Payroll (EHRP) system.

The EHRP is a Department of Health and Human Services initiative to replace its existing human resources (HR) and payroll system (known as IMPACT) with the EHRP system. The new system is based on PeopleSoft's web-based HR management system for the federal government.

The EHRP system provides a tool for: NIH

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## HIGHLIGHTS

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Serendipity and Sweat in Science

## 'Frog Man' Daly Follows Curiosity To Ends of the Earth

By Anna Maria Gillis

When he first contacted NIDDK's Dr. John W. Daly in 1990, John Dumbacher says he was afraid that the senior scientist would think "I was just a nutty kid."



But Dumbacher, then a graduate student in ornithology at the University of Chicago, needed the help of one of the world's leading natural product chemists to test what seemed a far-fetched idea.

Although there was nothing in the scientific literature proving that birds could store noxious compounds for chemical

SEE DALY, PAGE 4

From *Sir, With Love (of Longer Life)*

## Peto Says Halving Premature Death Rate Is An Achievable Goal

By Rich McManus

There aren't many in medicine who can authoritatively offer prescriptions for the entire world, but Sir Richard Peto, who has built an internationally acclaimed career examining the big picture, from the vantage of medical statistics, may be one of them. Returning to NIH for the second time in a month (the first was to accept the 2002 Charles Mott Prize from the General Motors Cancer Research Foundation), Peto explained, before a Wednesday Afternoon Lecture audience in Masur Auditorium on June 26, that halving the rate of premature death worldwide is within the capacity of current medical expertise.



The major culprits in causing

Sir Richard Peto meets with guests in the Special Events office before giving his talk in Masur Auditorium.

SEE PETO, PAGE 6



Dr. Sheldon S. Miller has been named NEI scientific director. Formerly a professor of molecular and cell biology at the University of California, Berkeley, he has focused his research on understanding the regulation and function of epithelial layers throughout the body, especially epithelia from the breast, lung and eye. He is also developing animal models of retinal disease to help establish therapeutic interventions. Miller has authored or co-authored more than 60 scientific papers, and has received continuous grant support from NIH since 1978. He is a member of several professional societies including the Association for Research in Vision and Ophthalmology, the American Physiological Society, and the Biophysical Society.

#### WILSON, CONTINUED FROM PAGE 1

century. In his book, Wilson unveils a plan to conserve Earth's natural biological diversity, and makes a passionate plea for quick and decisive action.

With the new book as the basis of his lecture, Wilson will discuss his extensive research, and his plan for the rescue of Earth's biological heritage. In the process, he will explore ethical and religious bases of the conservation movement and challenge the idea that environmentally sound policy cannot coexist with economic growth.

Wilson earned B.S. and M.A. degrees in biology from the University of Alabama, and a Ph.D. in biology from Harvard University. He joined the Harvard faculty in 1956 as a researcher and professor of zoology, specializing in entomology. Among his accomplishments is the development (with Robert H. MacArthur) of the theory of biogeography, a basic part of modern ecology and conservation biology, and the creation of the discipline of sociobiology, in 1975. Wilson also edited the 1988 volume *Biodiversity*, which introduced the term and drew worldwide attention to the subject. This volume and Wilson's book, *The Diversity of Life*, published in 1992, assembled knowledge about the magnitude of biodiversity and the



Dr. Edward O. Wilson

growing threats to it. His subsequent book, *Consilience: The Unity of Knowledge* (1998), brought together the sciences, humanities and the arts into a broad study of human knowledge.

Wilson has written more than 370 articles, and published 21 books, two of which have been awarded Pulitzer Prizes—*On Human Nature* (1978) and *The Ants* (1990, co-authored with Bert Hölldobler).

He has received over 75 awards internationally for his contributions to science and humanity, including the National Medal of Science. For his conservation work, he has been awarded the Audubon Medal of the National Audubon Society and the Gold Medal of the World Wide Fund for Nature. Wilson is also a member of the National Academy of Sciences and the Royal Society of England, and a recipient of 27 honorary degrees from North America and Europe.

The lecture is part of the NIH Director's Wednesday Afternoon Lecture series. For more information or for reasonable accommodation, call Hilda Madine, 594-5595. ■

#### EHRP SYSTEM, CONTINUED FROM PAGE 1

leadership to manage the NIH workforce strategically; minimizing reporting discrepancies; reducing duplicate data.

Implementation of the system will enable HHS to: enhance payroll operations; manage both vacant and filled positions; reduce paper and minimize redundant systems.

EHRP end users can look forward to an opportunity to use the latest web-based technology and increased data accuracy.

NIH'ers will still have access to Employee Express and should not experience any changes as a result of the EHRP implementation.

The HHS Program Support Center is providing EHRP training for NIH end users through Sept. 6. The EHRP system is scheduled for implementation on Sept. 9. For more information visit <http://ehrp.nih.gov/>. ■

#### NIH Hosts Pavilion at Black Family Reunion

As part of its outreach efforts to address health disparities, NIH will participate in the 17th annual National Black Family Reunion Celebration Sept. 7-8 on the grounds of the Washington Monument. NIH has reserved a pavilion to educate the public about its commitment to conduct and support research that will result in improved health for all people. The National Council of Negro Women reunion attracts more than 500,000 people. All are welcome to attend. Admission is free. For more information about the NIH exhibit, call Joan Lee of NEI (496-8990), Levon Parker of NINDS (496-5332) or Frederick Allen Whittington Jr. of OD (594-3591). ■

## NIH RECORD

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## 'Medicine for the Public' Lectures Begin 26th Year

The 2002 Medicine for the Public lecture series, now in its 26th year, features physician-researchers working on the frontiers of medical discovery at NIH. The series helps people understand the latest developments in medicine with an emphasis on topics of current relevance presented by speakers who can relate stories of science to the lay public. Sponsored by the Clinical Center, the lectures are held at 7 p.m. on Tuesdays in the CC's Masur Auditorium. All lectures are free and open to the public.

**Sept. 17, "Bioterrorism"**—Dr. Pierre Noel, chief, hematology, CC department of laboratory medicine, will present the recent history of biological warfare programs, which offers a perspective on what the future may hold. He will also discuss the biologic and physical characteristics that may render a biological agent a potential weapon.

**Sept. 24, "The Genetics of Speech and Communication Disorders"**—Dr. Dennis Drayna, senior fellow, section on transcription factors, sensory receptors and channels, Laboratory of Molecular Biology, NIDCD, will explain how genes affect the ability to communicate. He will discuss his work with stuttering and disorders of pitch recognition—also known as "tone deafness."

**Oct. 1, "Coping with Anxiety and Depression in Uncertain Times"**—Dr. Dennis Charney, chief, Mood and Anxiety Disorder Experimental Therapeutics and Pathophysiology Branch, NIMH.

Recent research indicates that severe psychological trauma can cause symptoms of anxiety and depression. Charney will discuss these symptoms and how they affect brain function and alter body systems,

and explore current treatments available.

**Oct. 8, "Nutritional Therapies for Age-Related Eye Diseases"**—Dr. Emily Chew, deputy director, Division of Epidemiology and Clinical Research, NEI, will explain age-related eye diseases, their incidence and the results of recent studies regarding nutritional supplements for these conditions. The public health impact of such treatment will also be assessed.

**Oct. 15, "The Teen Brain"**—Dr. Jay Giedd, chief, Brain Imaging, Child Psychiatry Branch, NIMH, will explore recent findings from brain imaging (there is evidence, for example, that the brains of 9-year-olds differ from those of 13-year-olds) and the implications these findings have for parents, teachers, society and the teens themselves.

**Oct. 29, "Endometriosis: Scrambled Eggs and Killer Cramps"**—Dr. Pamela Stratton, chief, Gynecology Consult Service, Pediatric and Reproductive Endocrinology Branch, NICHD, will explain a study investigating whether raloxifene will prevent the return of pain after surgical treatment of endometriosis. What sets this research apart is the study of a designer estrogen, which blocks the body's estrogen in the uterus and therefore may prevent the regrowth of endometriosis.

For more information, contact Dianne Needham, 496-2563, or visit <http://www.cc.nih.gov/cc/mfp/series.html>. ■



## Workshop on Burden of Skin Diseases

NIAMS is sponsoring a workshop on the burden of skin diseases Sept. 4 and 5 in Lister Hill Auditorium, Bldg. 38A. A diverse group of experts in dermatology, epidemiology, data systems, economics, health services and public policy will examine elements that comprise the burden of skin disease, the impact on public health and daily living, current knowledge and data collection instruments and future data needs.

For more information, call Laura Livingston at (202) 973-8724 or email [burdenskin@courtesyassoc.com](mailto:burdenskin@courtesyassoc.com).

## Children's Inn Needs Overnight Volunteers

Overnight resident volunteer managers are needed to staff the Children's Inn during Sunday through Thursday evening shifts. Volunteers typically serve one or two times every couple of months, managing the inn from about 8 p.m. to 7 a.m. Volunteers will receive inn operations and procedures training and will reside at the inn during their experience as onsite hosts, facilitators and managers. For more information, call Laura King, director of volunteers, 496-5672 or email [lking@box-l.nih.gov](mailto:lking@box-l.nih.gov). ■

## FEW Holds Meeting, Sept. 10

The Bethesda chapter of Federally Employed Women (FEW) will host a brown bag meeting on Tuesday, Sept. 10 from noon to 1 p.m. in Bldg. 40, Conf. Rm. 1201-1203. Alisa Green, program specialist for the NIH Work and Family Life Center and telework coordinator at NIH, will present results from a GSA study exploring the benefits of teleworking. All are welcome to attend. ■



Randy Schools (l), president of the NIH Recreation & Welfare Association, and Dave Smith (second from l), executive director of Special Love/Camp Fantastic, accept a check from Gary Daum and Steve Soroka (r) of the NIH Community Orchestra, who presented the gift to the R&W Foundation to assist with various patient needs on the NIH campus.

DALY, CONTINUED FROM PAGE 1

defense, Dumbacher was certain the flesh and feathers of the *Pitohui* contained toxins. While handling the bird in the field in Papua New Guinea, Dumbacher had cut his hand and licked the wound.



Daly (r) poses with former postdoctoral fellow Kenneth Seamon in 1983, shortly after they discovered that forskolin was a powerful research tool.

His mouth numbed. He also knew that the locals wouldn't eat what they called the "rubbish bird" unless it was skinned and specially prepared to make it safe.

Dumbacher sent samples to Daly and called every 3 months to track progress. "Around Thanksgiving, Daly called and said, 'We need more tissue. This looks like it's poisonous.'"

"No other chemists rose to the bait," says Daly of the bird project. The chief of NIDDK's section on pharmacodynamics didn't expect the birds to be especially toxic, but curiosity made him prepare and test the extracts anyway. "I injected them into a mouse, and within minutes it had convulsions and died," adds Daly.

Soon Daly began mentoring Dumbacher, and he worked on the project with chemists Thomas Spande and Martin Garraffo, two of his long-term NIDDK collaborators.

After Daly isolated the toxin, Garraffo did a mass spectrum and called Daly that weekend with the toxin's molecular weight and spectral analysis. The pattern of chemical fragments Garraffo described was one that Daly recognized right away—he had seen it before during analysis of compounds in extracts from skins of poison-dart frogs that he'd collected nearly 30 years before. "I knew this had to be a batrachotoxin," says Daly, still excited about making that connection. Finding the potent neurotoxic alkaloids in birds had defied his expectations.

"You don't know how serendipitous this was," adds Dumbacher. "Of all the natural product chemists in the world who could have looked at it, John did. Another lab might have taken a couple of years to figure out what it was." Since the *Pitohui* finding, the group has also found a range of batrachotoxins in another bird called *Ifrita kowaldi*.

Daly, who has been at NIH since 1958, hadn't planned on becoming an expert on bioactive alkaloids. But he got started on this research path in 1963 when Bernhard Witkop, then his lab chief, asked him to go to western Colombia to work on toxins from poison-dart frogs. Daly thinks he was "an ideal person for this job because I'd always been interested in biology." As a child in Oregon, he collected frogs, snakes and lizards and kept terrariums in his basement so he could breed what he'd found.

Witkop wanted to study the frogs' chemistry, but

the cost of getting the frogs was prohibitive until Daly got involved. "NIH was paying me \$16 a day per diem—far, far less than what was being asked by professionals to collect in the dangerous rain forests of Colombia," says Daly.

The frogs collected near Río San Juan yielded several batrachotoxins, which were featured in a 1966 article in *Medical World News*. Charles Myers, then a herpetology graduate student in Panama, chanced upon that story. He wrote to Daly and proposed they collaborate on a study of related poisonous Panamanian frogs to determine whether bright coloration and toxicity are linked. The two have worked together ever since.

In fact, if Myers had never contacted him, Daly muses that his nearly 40 years of frog alkaloid work may have ended with his initial Colombian forays. "Without Chuck Myers, this program would never have happened. He came up with a great deal of the money for the field work, planned the logistics and worked on requisite permits."

Myers, now a world-renowned herpetologist based at the American Museum of Natural History in New York, sees his collaboration with Daly as one where a taxonomist and chemist taught each other. "I was interested in the taxonomic and evolutionary implications of the toxins, which also have novel pharmacological properties," says Myers. "Scientists talk about doing this kind of interdisciplinary work, but we don't often see it."

Myers taught Daly how to use museum collection records, some dating back to explorations in the 1800s, to pick field sites. "You see someplace from where 20 or 30 frogs were preserved and you know where to go," says Daly.

To get to their gathering sites, the researchers have traveled by jeep, pack animal and dugout canoe and on foot. "Our field work was not to biological research stations, but to quite remote areas," says Myers. Initially, this concerned Myers, who feared Daly would get lost. It was an unfounded worry: "John has a built-in compass."

Once in the field, the two had a simple test to decide whether to take a particular frog. "It involved touching the frog, then sampling it on the tongue. If you got a burning sensation, then you knew this was a frog you ought to collect," says Daly. A healthy sense of self-preservation did prevent them from tasting *Phylllobates terribilis*, a Colombian frog the locals handle with caution because a single one contains enough batrachotoxins to kill a dozen or more people.

The frogs Daly, Myers and their colleagues eventually collected cover a wide territory—Panama, Colombia, Ecuador, Peru, Venezuela, Brazil, Argentina, Madagascar, Australia and Thailand—and their skins have yielded more than 500 natural substances, mainly alkaloids that the animals picked up

from their diet of ants, millipedes, beetles and other arthropods. "The frogs are much better bioprospectors than I am," says Daly. "They're the ones that found the chemicals in the arthropods."

"When we got started, there was only one alkaloid known in a vertebrate and that was samandarine from the European fire salamander," says Daly. Initially, he thought that the frogs made their own alkaloids because scientists who grew the salamanders in captivity said the salamanders produced the alkaloids on their own, a belief that threw Daly off track for a while. "One frog can have as many as 70 different alkaloids," says Daly. "Certainly, they wouldn't have the separate biosynthetic machinery for all of them."

Myers says Daly was "dogged" in his determination to learn the source of the alkaloids. Daly says he, like most scientists, was initially skeptical that the alkaloids came from an environmental source. To test whether animals acquired or made their own chemical defenses, Daly and colleagues took captive-raised frogs that had no alkaloids in their skin and fed them crickets dusted with alkaloids from wild frogs or with leaf-litter insects. The frogs fed alkaloid-laced crickets did indeed sequester the alkaloids in their skin. More recently, Daly and his colleagues have shown that one group of Australian frogs make one type of alkaloid and sequester another type that they get from their environment. That various unrelated frogs and toads have developed the ability to sequester alkaloids indicates the importance of chemical defense in their evolution, says Daly.

For all his interest in field biology, Daly considers himself a pharmacologist with a strong background in chemistry. He trained as an organic chemist at Stanford University and as a pharmacologist with Julius Axelrod. Early in Daly's NIH career, he worked with Axelrod on catecholamines and many aspects of drug metabolism, which was useful training for Daly's future work on animal-derived alkaloids. "I learned pharmacology and physiology from a real master," says Daly. "He instilled in me an appreciation for designing simple experiments to probe complex questions."

Four classes of alkaloids—the batrachotoxins, histrionicotoxins, pumiliotoxins and epibatidine—discovered by Daly have remarkable biological activity on specific ion channels essential to nerve and muscle function.

Daly and his colleagues demonstrated that batrachotoxins selectively opened sodium channels that control nerve and muscle cells. They then modified a batrachotoxin to make a radioactive analog. Scientists now use this radioactive probe to study whether and how local anesthetics, anticonvulsive drugs and other medicines attach to sodium channels.

Daly's group showed that pumiliotoxins have potential as heart stimulants because of their effects on the ion channels in that organ. They also demonstrated that epibatidine, a trace alkaloid from an Ecuadorean frog, was 200 times more potent than morphine as a painkiller, and that it acts not through morphine-sensitive targets, but through receptors for nicotine. Many syntheses of this potent alkaloid have been developed in labs around the world, and one analog made it into clinical trials for the treatment of chronic pain. "I'm a firm believer that if you find a compound that will target one macromolecule, then you'll be able to learn something important," he says.

Daly, a National Academy of Sciences member, has received many honors for his work. Most recently, the American Chemical Society gave him the 2002 Ernest Guenther Award in the Chemistry of Natural Products. The award cites his "pioneering contributions to natural product chemistry, organic chemistry, enzymology, neuropharmacology, membrane biology, and evolutionary herpetology, which are truly without equal in contemporary science."

Intellectual curiosity is the driving force behind Daly's approach, says his colleague Spande. He likes "research that answers some nagging question that may first appear to be tangential or even inconsequential to the main mission."

For instance, "John did not dismiss out of hand, as many would have, the possibility that any bird could be toxic, but was willing to take the time to check this unlikely hypothesis, and bingo, the world now had a major, fascinating (but initially controversial) problem in chemical ecology to wrestle with," says Spande.

This tendency of Daly's to challenge more popular hypotheses is what makes "him true to the scientific way," says Dr. Kenneth Seamon, vice president of drug development for Immunex Corp. and a former postdoctoral fellow in Daly's lab. Seamon worked with Daly on what some scientists consider his most far-reaching work. Together, they discovered that forskolin, a cardioactive chemical from the *Coleus* plant, could activate one of the most important enzymes in the body. The enzyme adenylyl cyclase stimulates production of cyclic AMP, which, in turn, controls many biochemical reactions in cells. Their discovery that forskolin could be used to increase cyclic AMP levels gave scientists a much-needed way to determine the physiological and pharmacological role of cyclic AMP in organs, tissues and cells.

Seamon learned three things from his mentor that he practices today: Don't prejudice what a scientific outcome will be, collect a lot of information before



*In 1973, Daly collected toxin-containing frogs near Río Saija in western Colombia. Skinning the poison dart frog *Phyllobates terribilis* required protective gear.*

### Tae Kwon Do Beginner's Class

The NIH Tae Kwon Do School is offering a beginner's class for adults and mature teens starting Sept. 9. The class will meet in the Malone Center (Bldg. 31C, B4 level, next to the NIH Fitness Center) from 6 to 8 p.m. on Mondays and Wednesdays, and will continue for approximately 2 months until participants can be integrated into the regular school training. For information, call Andrew Schwartz, 402-5197, or visit online at <http://www.recgov.org/r&w/nihtaekwondo.html>.

DALY, CONTINUED FROM PAGE 5

drawing a conclusion and integrate disciplines. "It is astounding how [Daly] combines biology, chemistry, biochemistry and pharmacology. His ability to integrate is unique."

Besides intellectual breadth, Daly has other abilities that contribute to his success. His colleagues universally comment on his capacity for long hours, his open door policy, and, as NIDDK's Martin Garraffo says, "his willingness to explain things to 'mere mortals.'"

Daly's work ethic was greatly influenced by Dr. Joseph E. Rall, who was NIDDK's scientific director when Daly was learning to be a scientist. "He told me 'Any good scientist spends 60 hours a week on it because he loves it,'" says Daly.

And there's more to research than the bench or field. "I feel strongly about the obligations of being a scientist," says Daly. Reviewing papers and giving feedback are high on the list. Rall gave him feedback regularly, and "I try to do the same with my group, maybe not always successfully, but I try."

"He takes being a mentor seriously," adds Dumbacher, now a Smithsonian Institution researcher. "He was always over my shoulder and made sure I didn't screw up the chemistry," says the ornithologist. Daly also guided Dumbacher to all the right papers, gave him advice on negotiating collection permit issues, encouraged him to learn what local people knew about an animal and helped him get his first major paper published. "There are lots of skills that students have to learn. John taught me what I needed to be professionally competent, not just a scientist."

Daly plans to stay at the bench and go into the field for as long as he can. He would have liked another chance to collect *Phyllobates terribilis* and find the source of its batrachotoxins, he says, "But it's too hard to get a collecting permit in Colombia now." He's shifted his collecting efforts to Madagascar and Thailand, where he has new frogs to find and new students to mentor.

Daly has no career regrets. He's liked NIH, and, even when other offers came he never thought seriously about them. "I love research so much that disrupting it to move someplace else has never appealed to me," he says. "NIH has been a blessing to me. I don't think I would have prospered in an academic world where I'd have to defend my research and lie about where it was going, because, in many cases, I didn't know where it was going to go." ■

### Stuttering, Speech Articulation Study

NIH seeks children ages 5-12 for a study to better understand stuttering and speech articulation disorders. There is no charge for those who take part. For more information, call 1-800-411-1222 (TTY 1-866-411-1010). ■

PETO, CONTINUED FROM PAGE 1

early death are smoking, preventable illnesses of childhood (tetanus, diarrhea, measles, perinatal complications), and vascular diseases for which there are solid, classical tools for diagnosis, and emerging therapies, chiefly statins, that are effective, said Peto, who is professor of medical statistics and epidemiology at the University of Oxford in England.

To hear Peto tell it, the only theoretically safe smoker is one who lights up just before facing a firing squad, beyond all hope of rescue; every other smoker is going to lose a percentage of expected lifespan every time he or she smokes. The only



*Peto (l) accepts commemorative statuette from NCI's Dr. Joseph Fraumeni. Peto gave the annual Robert S. Gordon, Jr. Lecture on June 26.*

difference between the condemned man and the habitual smoker is how far away, in time, the firing squad stands; eventually both perish early.

Peto began with a graph of the French mortality rate, from 1900 onward, showing that roughly one-quarter of the population died in early childhood, one-quarter died in early life, one-quarter perished in middle age (which he defined as "that period between youth and old age that is variously reckoned to suit the reckoner"), and one-quarter expired in late age. "Most of these deaths [in all categories but late-age] are avoidable," he suggested. Indeed, since 1950, the rate of premature death has diminished considerably. "The present is not as bad as the past," he said.

Comparing actual death rates in the 20th century to what we might expect in the 21st, Peto said about 20 million people are thought to have perished in the flu epidemic of 1918-1919 (though that could have been the number who died in India alone, he noted; 40 million or 50 million is probably the more accurate global guess). Another 200 million died in war, or war-related famine (the worst famine on record occurred 40 years ago in China, he said, when between 20 million and 40 million people are thought to have died). And 2,000 million died of preventable childhood diseases, including cholera.

Today, about 60 million people die per year, worldwide, and about twice that number are born. The deaths, early in the 21st century, occur as follows: About 10 million die in early childhood (though over the last 50 years, there has been a threefold reduction in childhood mortality, leaving

out the effects of HIV); another 10 million die in the age range 5-34 (again, excluding HIV numbers, which are expanding); and 20 million die in both middle age (35-69) and late age (70-plus). Peto thinks several of those age ranges are ripe for the halving.

The earliest age range is a good target, he said, because many childhood ailments are preventable. "But halving death at middle age is very hard due to HIV, an epidemic that is increasing fast," he said. Peto paused to condemn denial as a culprit in addressing AIDS adequately; those who don't believe HIV is the causative agent have only to examine a paper published in *Nature* in 1995 showing conclusively, among a population of severe hemophilia patients in Britain (half of whom were unwittingly infected by HIV when pooled blood harvested for clotting factor became tainted), that HIV is the cause of AIDS.

"HIV and tobacco are the only big causes of death still on the rise," he said. Of the 130 million people born this year worldwide, about 20 million will die before middle age, and some 40 million will die in middle age (20 million from vascular diseases—Peto warned of an alarming increase in obesity in China, India and North America that will elevate diabetes and its associated complications—and 10 million from cancer). "Can these be halved?" he wondered. "What can we actually do with our present knowledge? Well, we can take the known causes (of premature mortality) a bit more seriously."

Peto said that classical risk factors for heart disease—blood pressure, lipid profile and history of smoking—have an underestimated power as predictors of early death. A meta-analysis of 59 heart disease studies showed that each 20 mmHg difference in systolic blood pressure involved a two-fold difference in vascular mortality in middle age, he said. Both diastolic and systolic values "are very strong and very important determinants of the risk of vascular disease," Peto stated. "Both are more important than they are generally held to be."

Even modest downward tweaks in blood pressure are associated with real benefits, he added. Peto suggested that a strategy of many small interventions of a cheap and easy kind (aspirin, statins) would have a substantial cumulative effect. Of statins he joked, "One little pill can turn your cholesterol level from that of an American to a rural Chinese." With one-half of all adult deaths due to vascular disease, Peto urged a return to an emphasis on classical risk factors—not high-tech, expensive and hard-to-deliver diagnostics and therapeutics.

Turning to tobacco, Peto highlighted three main messages: The risk is big—half of those who smoke die by the habit; one-quarter of those die in middle age, losing many years of life; and if you quit smoking, you can salvage years that would have

been lost. "This ought to be common knowledge among smokers, but it's not," he protested.

Half of all cancer mortality in the U.S. was tobacco-related throughout the 1970's and 1980's, Peto said, but the rates are gently declining. He credited changes in cigarette composition as a significant factor in reducing the cancer death rate, but quipped that NCI hates to hear him acknowledge this.

The United Kingdom has also witnessed an "extraordinary decrease in lung cancer mortality" in the past half-century, he reported, but the trend is directly the opposite in France and Hungary, where smoking in both male and female populations is rising, with predictably dire results. Peto found it morbidly funny to have heard a Hungarian scientist rail against the perils of air pollution in his country, all the while puffing madly on a cigarette.

Smoking is also disastrously common in China, where two-thirds of adults smoke, and India, where 40 percent of the population smokes, Peto said. "If we keep going the way we are, there will be 1 billion tobacco-related deaths in the 21st century [compared with 100 million deaths in the 20th century]," he predicted. Adults need to quit, and the percentage of kids who start must be reduced, he prescribed.

The death rate from cancers not attributable to smoking has been halved in the past 50 years, Peto said, adding that "this could happen for other causes of death, too." The child survival rate also is improving, but needs substantial resources worldwide, he argued. His talk, given in honor of the late NIH epidemiologist Dr. Robert S. Gordon, Jr., ended whimsically: "Still, however, only a small proportion will survive to 100—halving premature death will not give us eternal life." ■

#### Hispanic Heritage Month Celebration Begins, Sept. 19

The NIH Hispanic Employee Organization will host the 2002 NIH Hispanic Heritage Month Celebration Part 1, "Language and Access to Care," on Thursday, Sept. 19 from 9 a.m. to 12:30 p.m. in Lipsett Amphitheater, Bldg. 10.

Following remarks by NIH director Dr. Elias Zerhouni and U.S. Surgeon General Richard Carmona, lectures will be given by Dr. Thomas Münte, Otto von Guericke University, "How To Handle Two Languages with One Brain: A Neuroscience Perspective"; Dr. Nilda Peragallo, president, National Association of Hispanic Nurses, "Language and Culture: Bridges or Barriers?"; and Dr. Carlos Zarate, chief of NIMH's mood disorders research unit, "Pilot Hispanic Research Initiative in Mood Disorder Patients."

An exhibit and reception follow the program until 2 p.m. in the B1C atrium of Bldg. 10. Sign language interpretation will be provided. For reasonable accommodation, contact the NIH Office of Equal Opportunity and Diversity Management, 496-6301.

### Von Eschenbach Lectures Summer Interns

On July 11, jeans, sneakers, T-shirts and even a couple of baseball hats comprised the wardrobe of the crowd in Bldg. 1's Wilson Hall. Only one suit was to be seen—worn by National Cancer Institute director Dr. Andrew von Eschenbach, who gave the annual Director's Lecture to the class of 2002 Cancer Research Training Award (CRTA) interns.

"How many of you have ever been to Los Alamos?" he asked. Several hands went up. Von Eschenbach talked about Los Alamos in the context of moments of "strategic inflection," a concept he attributed to Andrew S. Grove. In his book, *Only the Paranoid Survive*, Grove discusses strategic inflection, which he explains as the time "when the balance of forces shifts from the old structure, from the old ways of doing business and the old ways of competing, to the new." Von Eschenbach compared the 20th century quest to understand the fundamental nature of matter, and the work in Los Alamos in particular, to today's quest to understand the cell; both he called "moments of strategic inflection."

The director then gave the students an overview of research at NCI and reminded them that they are in positions of great opportunity to help eradicate cancer. He sent the students back to their labs with: "I wish you the very best of luck. I wish I could switch places with you."

For the third year in a row, NCI's Office of Diversity and Employment Programs sponsored the lecture to honor summer science CRTA interns, numbering between 450 and 500 students. The lecture gives the interns an opportunity to meet one another, to meet the NCI director in a special setting, to be exposed to NCI leadership outside of the lab and to get a broader perspective on activities beyond their assigned lab or project.

"At other internships I've had, I never had the experience of a top level speaker discussing the importance of interns," said Chris Zalewski, a CRTA intern who attended the lecture. He is working on sequencing cat genes at NCI's facility in Frederick, Md. He said von Eschenbach's talk was very inspirational.

Adam Brandt, another intern at NCI's Frederick site, who will start his senior year in high school this fall, said the Director's Lecture was very interesting and informative. He has always loved biology. "I'm having a lot of fun," he said of his summer at NCI.—Elizabeth Saloom ■



NCI director Dr. Andrew von Eschenbach speaks to CRTA interns.



Ian Gifford displays his T-shirt from the Director's Lecture for the CRTA interns.

Dr. Michele Kiely recently joined NICHD as chief of the collaborative studies unit in the Division of Epidemiology, Statistics and Prevention Research. In this capacity, she has become scientific advisor to the NIH-D.C. Initiative to Reduce Infant Mortality in Minority Populations in the District of Columbia. Her research



interest is the application of epidemiology to public health practice. She plans and conducts research that seeks to reduce the high infant mortality rate in the District. Her professional experience includes positions as research scientist at the New York State Institute for Basic Research in

Developmental Disabilities; epidemiologist at the Division of AIDS, NIAID; chief epidemiologist at the Maternal and Child Health Bureau, HRSA; and director of the Cincinnati pediatric research group, Cincinnati Children's Hospital and University of Cincinnati. She is currently the American co-editor of Paediatric and Perinatal Epidemiology.

### Chamber Music Concert, Sept. 8

The Rock Creek Chamber Players will begin their tenth season of performances at 3 p.m. on Sunday, Sept. 8 in the Clinical Center's 14th floor assembly hall. The free public concert, sponsored by the recreation therapy section, will include Telemann's Gulliver Suite for two violins, Krommer's quartet in B flat for bassoon and strings, Ravel's sonata for violin and piano and Copland's nonet for strings. For more information call (202) 337-8710. ■

### Wednesday Afternoon Lectures

The Wednesday Afternoon Lecture Series—held on its namesake day at 3 p.m. in Masur Auditorium, Bldg. 10—features Dr. Edward O. Wilson on Sept. 11 (see story on p. 1).

On Sept. 18, Dr. Elizabeth A. Komives will speak on "Biophysics of Protein-Protein Interactions." She is professor, department of chemistry, University of California, San Diego.

For more information or for reasonable accommodation, call Hilda Madine, 594-5595. ■

### Trauma Survivors Sought

Volunteers are needed for research studies looking at how people respond to and cope with a traumatic experience. Studies for people over 18 years old may include brain imaging, measurement of stress hormones and a free trial of commonly used medications for eligible participants. Compensation available for select studies. Call 1-866-MAP-NIMH (1-866-627-6464) or TTY 1-866-411-1010. ■