

# nih record



ABOVE • Though slated for removal soon, the crab apple trees outside NLM are still capable of drawing abstractions on both the sky and earth. See story on p. 12.

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*Common Myths, Misconceptions Addressed*

## Attention Deficit, Hyperactivity Explored In Depth at STEP Forum

By Carla Garnett

At age 5, Molly began keeping a secret about herself that she really didn't believe. Sure, she and her family, and even her teacher, had seen the signs. And yes, she often could feel her schoolwork suffer. But despite the fact—and in large measure, because—her father was a pro at identifying the symptoms in other children, Molly refused for years to accept what adults in her life were saying about her.

"Her mind seems to wander in the middle of a task and during instruction," her first-grade teacher wrote in a parent-requested evaluation. "Molly is easily distracted." Math—particularly when tackled in small groups—proved most challenging.

Molly was diagnosed with attention deficit/hyperactivity disorder that year, and



Dr. Alan Zametkin spoke at the recent STEP forum on attention deficit/hyperactivity disorder.

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## 2007 Budget Even with FY 2006

President Bush's budget request for NIH in fiscal year 2007, announced Feb. 6, totals \$28.587 billion, the same budget level as FY 2006.

Viewed in perspective, the FY 06 budget itself was notable as the first time since 1970 that NIH had a reduction in dollars relative to the year before. The bottom line for FY 06 stands at about \$60 million below that of FY 2005.

The FY 2007 President's request is therefore 0.2 percent below FY 05 and equal to FY 06.

Emphases within the President's 2007 budget include funding for several trans-NIH strategic initiatives: biodefense; enhanced support for new investigators; the NIH Roadmap for Medical Research; the Genes and Environment Initiative; the Clinical and Translational Sciences Award program; management innovations; and pandemic influenza.

In the field of biodefense, the budget calls for \$1.891 billion, an increase of \$110 million and 6.2 percent over FY 06. Within this increase, NIH will direct \$160 million to

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## Loving Family Relationships and Oxytocin A Cuddle a Day Keeps the Doctor Away

By Belle Waring

We mammals have it rough. Especially the humans among us. All mammals are born helpless—their survival hinges on maternal care—but compared to many other species, *Homo sapiens* require a prolonged childhood. Raising a human being is no joke.

Consider the mice of the field. A prairie vole (a critter resembling a mouse) weans its young at the tender age of 3 weeks or so, when the youngster departs to seek its fortune. But weaned human tots can't be cast out, so a lack of maternal bonding can be dire. It is, to put it mildly, a risk factor.

So, too, is an unhappy marriage.

This is a true-love story. It's about the rapport between mother and infant. It's also about romantic love—not the kind that made Romeo and Juliet risk everything, double or nothing, but rather the contentment they might have found with a longer-term deal. And it's about

SEE OXYTOCIN, PAGE 8



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**NIH Record Office**  
Bldg. 31, Rm. 5B41  
Phone (301) 496-2125  
Fax (301) 402-1485

**Web address**  
<http://www.nih.gov/nihrecord/>

**Editor**  
Richard McManus  
[rm26q@nih.gov](mailto:rm26q@nih.gov)

**Assistant Editor**  
Carla Garnett  
[cg9s@nih.gov](mailto:cg9s@nih.gov)

**Staff Writer**  
Belle Waring  
[bw174w@nih.gov](mailto:bw174w@nih.gov)

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## briefs

### Women's History Month Events

NIH's annual Women's History Month observance will include two events. The first, "Builders of Communities and Dreams," takes place Wednesday, Mar. 1 from 10 to 11 a.m. in Lipsett Amphitheater, Bldg 10. Edie Frazer, president and CEO of the Public Affairs Group, Inc., will be the keynote speaker. She developed Diversity Best Practices, Business Women's Network and Best Practices in Corporate Communications.

The celebration continues with a scientific symposium on Wednesday, Mar. 22 from 10 to 11 a.m. in Lister Hill Auditorium, Bldg. 38A. The highlight will be a panel discussion among winners of NIH Pioneer Awards.

Both events are sponsored by the Office of Equal Opportunity and Diversity Management. All are welcome to attend. Sign language interpreters will be provided. For information, call Glenda Keen (301) 496-5089. Individuals with disabilities who need reasonable accommodation should call Carlton Coleman at (301) 496-2906, voice or (301) 451-2290 (TTY).

### STEP Forum on Innovative Technologies, Mar. 9

The staff training in extramural programs (STEP) committee will present an Administrative Strategies forum on the topic, "Eureka! We Found IT (Innovative Technologies)!" on Thursday, Mar. 9 from 8 a.m. to noon in Lister Hill Auditorium, Bldg. 38A.

We're living in a time when scientific discoveries and technological innovation appear to occur at an exponential rate. But what is innovation? Is it cyclical or dependent on the presence of exceptionally creative individuals? What factors influence or foster the adoption of new technologies that change current paradigms and challenge existing models? Why do some discoveries lead to landmark successes, while other discoveries fade into the background? This forum will look at innovation from perspectives of basic science, translation and commercialization. Learn what NIH and others have done to foster innovation, and what more you and NIH can do to further develop and implement initiatives, policies and practices that promote groundbreaking and innovative biomedical research.

### Learn How To Write a Résumé

The Work and Family Life Center will hold a seminar titled "Résumé Writing" on Wednesday, Mar. 8 from noon to 2 p.m. at 6001 Executive Blvd., Rm. C. Does the thought of revising your résumé (or writing one for the first time) overwhelm

you? If so, this is the workshop for you. Attend this session and learn the fundamentals of résumé writing and how to connect your skills, knowledge and abilities to a future position.

### NIH Sailing Association Open House

The NIH Sailing Association invites everyone to its open house on Thursday, Mar. 2 from 5 to 8 p.m. at the FAES House on the corner of Old Georgetown Rd. and Cedar Ln. Would you like to learn to sail? Can you imagine being part of a group filled with skilled sailing instructors, enthusiasts and boat owners? Membership includes instruction, sailboats for charter, racing, cruises, parties and fun. Admission to the open house is \$5 at the door and includes pizza and soda. For more information visit [www.recgov.org/sail](http://www.recgov.org/sail).

### NIH Golf Association Seeks Members

The NIH Golf Association (18-hole coed league) is looking for new members for the 2006 season. We currently have seven teams of up to 25+ players each and schedule eight spring/summer stroke-play outings, plus up to five match-play outings each year at local courses (all mid-week and play is optional). We cap the year off in October with an outing including golf/cart/food for all members and their guests. Prizes and trophies are awarded and handicaps are maintained from 0-40, so all interested golfers are welcome. For more information contact Howard Somers at [somersh@mail.nlm.nih.gov](mailto:somersh@mail.nlm.nih.gov) or visit <http://www.recgov.org/nihga/>.

### Women's Baseball Team Needs Players, Coach

A women's baseball team consisting primarily of players from NIH is looking for new players and a coach. The Lasers are located in Rockville and play in the Eastern Women's Baseball Conference. They play one game most weekends, May to September, on a regulation ballfield with professional umpires.

The team will train locally in the coming months, indoors and outdoors. The Lasers have a core roster of women 18-52 years old, from all walks of life, and with a range of previous baseball and/or softball experience. If you are interested in playing or coaching, contact Susan McCarthy at [mccarths@mail.nih.gov](mailto:mccarths@mail.nih.gov).

## NHGRI, NIEHS Take 'Major Step Forward' for Medicine

By Colleen Chandler

NIH director Dr. Elias Zerhouni, along with Dr. Francis Collins, director of NHGRI, and Dr. David Schwartz, director of NIEHS, announced two new initiatives that will take advantage of recent technological advances to move health care research to the next level.

Zerhouni described the next level as the "Three Ps" of medicine: predictive, personalized and preemptive.

"We have not yet found the very fundamental molecular events that start the disease process," Zerhouni said at a press conference Feb. 8 at the National Press Club. "The paradigm has always been to wait for somebody to be struck by a disease, and then we intervene to bring that patient back from illness to health. The vision has always been to alter that process, to understand enough of the fundamental determinants of disease, understand their regulation, understand their interaction with the environment, and hopefully, to usher in a new era in medicine."

HHS Secretary Mike Leavitt announced Feb. 6 that the President's fiscal year 2007 budget calls for \$40 million a year for the multi-year Genes and Environment Initiative. The GEI will combine genetic analysis with the development of new environmental monitoring technology to accelerate research on common diseases such as asthma, arthritis and Alzheimer's disease. Collins and Schwartz will serve as co-chairs for the GEI coordinating committee.

The FY 2007 budget represents a \$40 million increase above the \$28 million already planned for these efforts in the NIH budget. Of the first year's funding, \$26 million will go to genetic analysis and \$14 million for the development of new tools to measure environmental exposures that affect health. As a result, GEI will have two main components: a laboratory procedure for efficiently analyzing genetic variation in groups of patients with specific illnesses, and a technology development program to devise new ways of monitoring personal environmental exposures that interact with genetic variations and result in human diseases.

The other initiative, the Genetic Association Information Network, is a partnership between private industry and government researchers to determine genetic contributions to seven common diseases, and includes pledges of \$25 million from Pfizer and Affymetrix. Run by the Foundation for the NIH, this initiative includes plans to raise more money from private industry



**Top:**

On hand at the Feb. 8 press conference were (from l) NHGRI director Dr. Francis Collins, NIH director Dr. Elias Zerhouni and NIEHS director Dr. David Schwartz.

**Bottom:**

Schwartz models a formaldehyde monitor, an example of a wearable device, a more extensive version of which NIEHS intends to develop as part of the GEI.

and non-profit organizations to fund research on additional diseases. Zerhouni said the GAIN initiative complies with one of the objectives of the NIH Roadmap for Medical Research: accelerating public-private partnerships.

The GEI and GAIN initiatives will affect both the scientific community and the public health community, Zerhouni said. With 75 percent of the nation's health care costs associated with common chronic, long-term diseases, he said, the initiatives provide the nation's greatest hope to control these skyrocketing health care costs.

Both the GEI and the GAIN initiatives focus on genetic analysis of single nucleotide polymorphisms, or SNPs, that normally occur within the 3 billion DNA base pairs that make up a person's genome. While most of the genetic variations are biologically meaningless, one-tenth of 1 percent of these SNPs alter the function of a gene, and the combination of many slightly altered genes may significantly increase the risk of developing a specific disease, according to an HHS press release.

Data gained from the new initiatives will be freely available for the scientific community. The National Center for Biotechnology Information, part of the National Library of Medicine, will maintain databases to manage the vast amount of data generated by these initiatives. The data, in turn, will be available to researchers in public and private sectors, NIH officials said.

"Both initiatives promise to rapidly identify the myriad genes in an individual that, taken together, contribute to an increased risk of illness—or that increase the chances of a healthy life," said Collins. "As the genetic underpinnings of health and common diseases become clearer, researchers will be empowered to develop targeted treatments that either prevent illness from occurring or treat it effectively once it does."

The GEI initiative will provide \$14 million a year to develop high-tech tools to measure environmental exposure and the biological responses to these exposures. These new tools could include small, wearable sensors, Schwartz said. ●

## NIH BUDGET

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an advanced development fund supporting efforts to work with academia and industry to develop candidate countermeasures from the point of investigational new drug applications to the level that these might qualify for acquisition by Project BioShield.

NIH will invest \$15 million in a new “Pathway to Independence” program to provide increased support for new investigators (see *NIH Record*, Feb. 10, 2006).

The Roadmap for Medical Research has three themes: New Pathways to Discovery (slated for \$181 million); Multidisciplinary Research Teams of the Future (to receive \$81 million); and Re-engineering the Clinical Research Enterprise (\$181 million). NIH will direct a total of \$443 million towards Roadmap initiatives, an increase of \$113 million over the FY 06 appropriation. This total arises from a \$111 million contribution from the NIH Director’s Discretionary Fund and \$332 million contributed by the NIH institutes and centers. The IC contributions represent 1.2 percent of each individual budget request for FY 07.

NIH also allocated \$40 million to the ICs to support a Genes and Environment Initiative, a multi-year plan to identify major genetic susceptibility factors for common diseases like heart disease, stroke, osteoarthritis, cancer, diabetes, and Alzheimer’s disease, while developing technologies to assess risk factors in diet, physical activity, and environmental exposure. This plan was announced Feb. 8 at a joint press conference held by NHGRI and NIEHS (see story on p. 3).

The Clinical and Translational Sciences Award program will combine existing NIH programs such as the General Clinical Research Centers in the National Center for Research Resources, as well as Roadmap initiatives in the Re-engineering the Clinical Research theme. Several full awards, as well as planning grants in FY 06 and 07 will increase as existing GCRCs complete current funding cycles and recompute these transformational awards. The FY 07 budget for this combined program is estimated to be \$361 million.

NIH will improve the management of its biomedical and behavioral research portfolio. The newly formed Office of Portfolio Analysis and Strategic Initiatives will develop methods to assist the agency in assessing its large and complex portfolio, coordinate trans-NIH evaluation efforts and provide a transparent process for identifying important scientific initiatives that cut across or fall between missions of institutes and centers.

A link to a summary of the FY 07 President’s budget can be found on the NIH home page under Medical Research Issues. 



### Brodsky To Give Annual Pittman Lecture, Mar. 1

By Kathy Stover

The roles of clathrin, an intracellular protein, in cellular communication and the immune response are the focus of this year's

Margaret Pittman Lecture. It will be presented by Dr. Frances M. Brodsky, professor of biopharmaceutical sciences, immunology, microbiology and pharmaceutical chemistry at the University of California, San Francisco. The lecture will be given Wednesday, Mar. 1 at 3 p.m. in Masur Auditorium, Bldg. 10.

During her talk, "Evolution of Membrane Traffic: Intelligent Design or Not?" Brodsky will examine the evolution of the clathrin protein from a structural point of view and the evolution of its cellular function, including its role in the uptake and regulation of antigen receptors on both B cells and T cells, as well as new research examining the protein's role in muscle.

An immunologist, Brodsky has helped bridge the gap between immunology and cell biology by using monoclonal antibodies to understand and characterize clathrin. The protein's name stems from the Greek word "clathrate," meaning "basket-like," reflecting the protein's basket-like structure.

As a doctoral student at England's Oxford University, Brodsky applied the new technology of monoclonal antibodies to study human histocompatibility molecules. During postdoctoral research at both Harvard University and Stanford University, she and her colleagues produced the first clathrin monoclonal antibodies, which led to the creation of reagents that are still widely used today. Further, she and her colleagues discovered the important role clathrin plays in transporting histocompatibility molecules and their stimulation of an immune response.

Brodsky received a B.A. with honors in biochemical sciences from Harvard in 1976. In 1979, she was awarded a D.Phil. degree for her doctoral research at Oxford's genetics laboratory. After 3 years of postdoctoral research, she joined Becton Dickinson Immunocytometry Systems in California in 1982 and established her own laboratory. In 1987, she returned to academic life as an assistant professor at UCSF. She became a full professor at the university in 1994.

Brodsky has written three science-related murder mysteries under the pen name B.B. Jordan. In 2000, she and three colleagues cofounded *Traffic*, the international journal of intracellular transport. No stranger to NIH, Brodsky served as a member of the board of scientific counselors for NIAID from 1998 to 2004 and has participated in several ad hoc committees designed to evaluate NIH programs. She is a member of the American Association of Immunologists, the American Society for Cell Biology and the Biochemical Society of the United Kingdom and is the author of hundreds of journal and textbook articles.

The lecture honors Dr. Margaret Pittman, NIH's first female lab chief, who made significant contributions to microbiology and vaccine development, particularly in the areas of pertussis and tetanus, during her long career at NIAID.

The lecture is part of the NIH Director's Wednesday Afternoon Lecture Series.

For more information, contact Sandeep Nair at (301) 496-1921. 📞



### Snowy Day Invites Impromptu 'Winter Olympics'

How better to enjoy a lunch break on a wintry day than to embark on some impromptu sledding with home-made sleds? NIMH employees (top, from l) Caitlyn Liebig, Jackie Klaver and Dara Cannon of Bldg. 15K proved up to the challenge on Feb. 13, fashioning luges from cardboard boxes augmented with plastic bags to reduce friction. You won't see rigs like this at the Winter Olympics in Turin, Italy, but they do just fine on the hill opposite the Clinical Research Center. Below, Klaver spins out halfway down the run.

## ADHD FORUM

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now at age 17½ she was on stage at an NIH STEP forum sharing the secret she'd been too afraid would label her as one of her dad's "mental patients." The picture of a healthy, successful high school student/athlete, Molly gave one

of four presentations on ADHD at a Jan. 10 conference in Natcher auditorium.

"I have regrets about the way I handled my ADD diagnosis," Molly admitted, recalling that at first, her parents tried to ease her symptoms with behavior modification. That's because Molly had refused all medication. Taking ADHD drugs, she reasoned, would mean she had

the disorder. But by third grade, Molly was taking a prescription stimulant to manage the ADD. (ADHD and ADD often are used interchangeably. Although many girls with the disorder, like Molly, do not seem to experience the hyperactivity component, the disorder officially is known now as ADHD.) She seemed to accept the reality of her condition in 8th grade, when she no longer had to be reminded to take her meds. It took the youngster several more years before she felt comfortable enough to reveal her ADHD to peers, but she had realized the disorder was affecting her life.

"I felt as though my ADD was affecting my future and my ability to learn," Molly said.

### Significant Effects on Family, Society

NIMH's Dr. Judith Rumsey, who moderated the forum, put the disorder in perspective. "ADHD is highly heritable and spans a range of severity and varies in its presentation," she said. It affects about 5 percent or more of school-age children in the U.S., but is by no means solely a kid's disorder. Contrary to popular belief, many children do not outgrow it, but continue to have impairing symptoms through adulthood. "Chances are that you personally know someone with ADHD—a child, adolescent, or adult, maybe a coworker," Rumsey said.

The effects of the disorder are significant for

those who have it as well as for their families and communities. Consider, for example, that 50 percent of adults with ADHD are also smokers. "It's one of the ways people self-medicate for ADHD," pointed out Dr. Xavier Castellanos, director of the Institute for Pediatric Neuroscience at New York University. "It's a very addicting way to treat oneself."

Motorists with ADHD are more prone to car accidents, according to Dr. Alan Zametkin, an NIMH senior staff physician and Molly's dad. In addition, the disorder often results in accidental injury. Workplace issues frequently emerge as coworkers with ADHD may tend not to finish projects they start. Problems in marriages and other personal relationships are also reported more by couples in which a partner has the attention disorder. About one-third of people with ADHD may also struggle with another learning disability, such as dyslexia.

### Diagnosis Is Judgment Call

One challenge to understanding ADHD is the way it is diagnosed, noted Zametkin. So far, there's no blood test or brain scan to clue in doctors, he said. In fact, there is no biological test of any kind to confirm the disorder. Instead, to determine if someone has ADHD, doctors use several criteria:

- Symptoms must be present for 6 months;
- Some symptoms should be noticed in children before they are 7 years old;
- There needs to be significant impairment or performance problems, and the problems should be seen in more than one setting (for example, at home and at school or the office); and
- Other mental disorders—anxiety, obsessive-compulsive and substance abuse, for instance—should be ruled out first.

"The key is the word impairment," Zametkin explained. "We need impairment to make a diagnosis. Some kids have it and are not diagnosed with it because their environments have been so modulated that the ADHD is not an impairment...If it's mild, we'd never treat it. It requires a fair amount of judgment."

### 'Fidgety Phil... Won't Sit Still'

Doctors rely heavily on information contained in a person's medical and family history, and school report cards from kindergarten through grade 5, to decide who has ADHD. The signs of hyperactivity are easy to spot: a person squirms excessively, can't stay seated, runs/climbs too much, can't play or work quietly, talks all the



Presenters at the ADHD forum include (from l) Dr. Alan Zametkin, Molly Zametkin, Dr. Maureen Donnelly, Dr. Xavier Castellanos and Dr. Judith Rumsey.

PHOTOS: ERNIE BRANSON



Castellanos details state of ADHD science.

time, interrupts conversations and can't wait turns. Symptoms of inattention may be more subtle: An individual is careless, doesn't listen, can't organize, loses important items, is easily distractible, doesn't

follow tasks through to completion and is forgetful in daily activities.

In adults, the most telling observations often come from spouses and other family members sharing daily life. Not surprisingly, perhaps, children and teens are not likely to see attention problems in themselves, although they may notice the results—poor performance on school assignments, for example.

These days, those involved in living with and treating ADHD often have a foe in addition to the disorder: public opinion. Some people think ADHD is an overdiagnosed ailment brought on mainly by a 1980s/90s society that overexposes its youngsters to home videos and computer games. Critics charge that U.S. pop culture overdiagnoses the ADHD and then compounds the problem by overmedicating kids believed to have it. After all, skeptics point out, ADHD only became “trendy” in the last few years or so, right?

Wrong, Zametkin countered. “I would argue that kids who have this problem have been around probably for centuries,” he said. “Clearly this is not a new disorder or a product of high technology or pharmaceutical companies.” He cited the first known description of ADHD dating back to an 1844 poem, *The Story of Fidgety Phil*, by German psychiatrist Heinrich Hoffmann. By 1903, U.S. pediatrician George Still was describing overactive children with discipline problems who seemed to have little control over their impulses. He attributed the disorder to a lack of morals, said Zametkin. In 1937, Dr. Charles Bradley reported remarkable improvement in the school performance of children with behavior problems who were given the stimulant Benzedrine. His work set the standard for treating ADHD with stimulants.

Nowadays the disorder—and its treatment—are talked about so commonly that myths and controversies often cloud understanding.

One particularly persistent myth is that some foods—for instance, chocolate or sugar—cause ADHD. Zametkin said researchers have not been able to link any dietary products to the disorder. Another unproven belief is that more boys than

girls have ADHD. Not necessarily true, said Zametkin. It may just be that more boys than girls are referred for treatment due to bias.

### Truth in Treatment

There is also skepticism in some circles about putting kids on prescription drugs to combat their ADHD symptoms, but the fact is ADHD medication works, acknowledged Dr. Maureen Donnelly, a former NIMH fellow and private-practice psychiatrist who specializes in treating ADHD. Research on ADHD drugs has taught us a lot in the past 30 years, she noted. Just 5 years ago, there were only four medications to treat ADHD; now there are 14. A patch that delivers therapy through the skin is also on the way, she reported.

“Medication treatment is one of our most powerful tools,” she stressed, sharing results of two NIMH-funded, multi-site clinical ADHD drug trials that together studied 700 children with the disorder.

Treatment has to be multifaceted, however. In addition to a drug regimen, if warranted, there should also be educational and vocational interventions for both the person with ADHD and the family. Psychosocial treatments and behavior modification, as well as vigilant monitoring of symptoms and function at home and school or workplace are also important components of effective therapy.

“We need to carry out what we know better,” she said. “And we have to deliver the medication in the best possible way.”

Castellanos agreed, noting “we don't have the best study that would show what treatment does over the long term—we may never get that—but we do have lots of evidence that lack of treatment is not a good thing.”

### Where Are We in ADHD Science?

While research on ADHD treatment has progressed a long way since the days of Benzedrine, there are a lot of things we still don't know about the disorder itself, according to Castellanos, who headed a unit on ADHD in Dr. Judith Rapoport's Child Psychiatry Branch, NIMH.

“We still don't know where in the brain the dysfunction happens,” he said. However, researchers do know that on average, people with ADHD have brains that are 4 percent to 5 percent smaller than non-ADHD brains. Also, MRI studies strongly point to the cerebellum, which integrates sensory perception with motor output.

We also know from studies of twins and of families with adopted children that ADHD is strongly inherited, Castellanos explained. “About 80 percent of causal factors are genetic and about 20 percent are environmental,” he said. As in most ailments, environmental and genetic factors interact to cause the disorder. For example, he said, smoking during pregnancy increases the likelihood of having an ADHD child. However, a woman who smokes while she's pregnant is probably also carrying genes that increase the risk of being a smoker and of having ADHD. “The environmental interactions cannot be disentangled” from the genetic factors, he stressed. Purely environmental factors—brain injuries sustained in a car wreck, for example—can cause ADHD as well.

Although researchers know genes play a critical role in ADHD development, the precise genes involved are not yet known. Castellanos said scientists suspect genes related to function of dopamine or norepinephrine, two naturally produced substances that affect brain function. In addition, researchers are looking at vulnerable brain relay points between feeling and thinking, and thinking and acting. Scientists think these points could be ADHD targets.

“We don't have the whole picture yet,” he concluded, “but we have more and more of a sense that we really are working out this gigantic multidimensional puzzle that is ADHD.”

NIH'ers can see the entire forum online at [www.videocast.nih.gov](http://www.videocast.nih.gov). 

## OXYTOCIN

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### Right:

*The beneficial effects of “the bonding hormone” on maternal blood pressure are now being measured. From the collection of U.S. Children’s Bureau c. 1945. Photo: Georg Jones. Courtesy National Library of Medicine.*

how maybe, if we’re lucky, we can cultivate that.

How do scientists analyze the effects of loving care on health? One way is to look at the role of oxytocin, a pituitary hormone, and measure its relation to blood pressure and heart rate, as well as to blood levels of stress hormones.

Oxytocin,  $C_{43}H_{66}N_{12}O_{12}S_2$ , is produced only in mammals. A peptide hormone which exhibits neurotransmitter-like actions, it has receptors in various sites, including the cardiovascular system. In the female body it stimulates the contraction of uterine muscle and the secretion of milk. Discovered at the turn of the 20th century, it was eventually synthesized in the 1950s and found clinical uses in labor, delivery and postpartum recovery.

Now Dr. Kathleen Light stands among the first scientists worldwide to study oxytocin in human social relationships. Funded through an NIH grant at the University of North Carolina, Chapel Hill, she recently traveled here to deliver her lecture “Loving Family Relationships and Oxytocin: New Human Findings.”

Light described oxytocin as “the bonding hormone” known to enhance pair-bonding in the 5 percent of mammals that are monogamous. Humans, she reminded us, are serially monogamous.

“If you are in love,” she explained, “that contact becomes rewarding because of pathways in the brain activated by oxytocin.” So if you give oxytocin to the females in a monogamous species like prairie voles, they are more likely to pair-bond with males. (Vasopressin, a related hormone, works this way on the males.) Oxytocin is also involved with social recognition and behavior, pain and stress regulation, mood and affect.

Light noted that there is extensive literature on animals and oxytocin, but “few studies look at oxytocin in humans, and even fewer in the context of social relations.” There have been human studies showing that social support is good for you, that marriage has a salutary effect on health, but these didn’t look at oxytocin.

She designed studies using “warm contact” in which couples sit close together, hips touching, in a love seat. They hold hands, talk to each other about a happy memory, then hug for 20 seconds.



Light found that the warm contact raised oxytocin blood levels in both men and women if they had supportive partners. These elevations were related to a decrease in blood pressure (BP) in women, but not, she said, in men.

Oxytocin levels were also linked to a reduction in women’s levels of the stress hormone norepinephrine but, again, not in men’s levels. “This makes us wonder: is oxytocin a more important regulator of stress responses in women?” she queried.

Her study couples were no strangers. They were monogamous co-habiting couples (not necessarily married) who had lived together for more than one year. Forty percent were African American; the rest were white.

“The benefit to the women’s blood pressure was linked to partner relationship quality, and to physical affection expressed as frequent partner hugs,” said Light. “Not all marriages are equally advantageous. It’s the relationship quality that determines if marriage has health benefits over being single.”

In a separate study monitoring BP and heart rate, Light found that warm contact had a positive effect across all race and gender groups. Men and women benefited equally, and even if the partner was no longer present, warm contact had an enduring effect.

Asked why she is among the first to study people this way, Light replied: “Many studies failed because they were trying to find an oxytocin change in response to a single event. It takes more than one exposure; it’s a cumulative effect of the way supportive couples habitually interact together and hug each other.”

Studying infants and mothers, Light found that mothers whose oxytocin increased after they held their infants closely showed lasting positive effects on the moms' blood pressure. Even without the babies present, the oxytocin's effect on maternal BP endured. She replicated the study and found that there was a much stronger effect if the infant was under 5 months.

Looking at prenatally cocaine-exposed versus non-exposed mother/infant pairs, she found that the cocaine-exposed mothers had lower oxytocin levels before and after baby contact, held their babies less at home and ran higher blood pressures. "They also had higher BPs in the lab except when they were holding their babies," Light noted. "Many of the mothers were bottle-feeders, but they were different from other bottle-feeders," she said. When interacting with their infants, or when separated briefly from them, as well as when exposed to tape-recorded baby cries or pictures of babies in danger, a second preliminary study showed that their oxytocin levels were consistently lower. They were also not as stressed during separation from their infants, but more stressed and overwhelmed when they listened to the tape-recorded baby cries, and interestingly, when seeing pictures of happy babies.

Because their oxytocin levels were relatively low, Light concluded, holding their babies was less rewarding and separation less aversive.

So why not give people oxytocin to enhance social behavior? "Last year's article in *Nature* by M. Kosfeld et al. showed that inhaled oxytocin in male subjects increased one kind of trusting behavior," she said, "but remember, oxytocin makes the uterus contract. And an uncontrolled decrease in blood pressure can be dangerous." She noted that nasal oxytocin administration approved for use in Germany may minimize adverse peripheral effects of oxytocin while allowing it to influence the brain.

But there are other, more hopeful, implications.

"There are implications for the mother-child bond," Light said. "Even in the cocaine-exposed mothers, the system was not broken. Their BPs decreased when instructed to hold their babies." Intervention is possible, she said.



*Le Mari Malade [The Sick Husband]. Lithographic print by Charles Motte, after A. Maurin, c. 1815. Courtesy National Library of Medicine.*

### Study Design Crucial in Couples Work

Studying human subjects can be tricky, since folks being observed may feel uncomfortable and behave in ways that are altered by the observation itself. When asked how she designed her studies, UNC's Dr. Kathleen Light offered these details: "There are lots of different ways to design the couple studies. We tried for a naturalistic setting, like couples sitting together at the movies. We also left the couples alone during their warm contact period so they would feel comfortable and behave normally. For the mother/baby interactions, we told the moms to behave as they usually do at home with their babies. This is one reason why our findings in the lab are linked to what happens at home—why how often the couples hug at home or how often the mom picks up her baby at home is related to the oxytocin and blood pressure measures we see in the lab studies. For these initial studies, being naturalistic was our highest priority. In future studies, we can examine whether it was the positive verbal interaction or the physical closeness and warm touch that was the specific component needed to see oxytocin differences."

### NIH Training Center Classes

The Training Center supports the development of NIH human resources through consultation and provides training, career development programs and other services designed to enhance organizational performance. For more information call (301) 496-6211 or visit <http://LearningSource.od.nih.gov>.

Cultural Diversity at NIH	3/6
Review, Update on EEO Policies and Processing Laws	3/6
Writing Statements of Work	3/7-9
Introduction to NIH Property Management	3/16-17
Purchase Card Training	3/20
Travel for Admin. Officers/Approving Officials	3/22
NIH Domestic Travel (NBS Travel System)	3/29-31

### Management Internship Program Accepts Applications Through Mar. 13

One of the challenges facing NIH today is identifying and training future leaders to successfully manage in a fast-paced, ever-evolving public sector. If you've thought about changing your career path or developing more depth and breadth of knowledge about NIH, the Management Intern (MI) Program may hold the keys to your future.

Entering its 49th year, the MI Program—a highly competitive 2-year rotational training opportunity—has graduated dozens of interns, many of whom now hold high-level managerial positions with NIH and other federal agencies. Outstanding men and women interested in a career in public service are encouraged to apply for the 2006 program.

Eligible candidates must be either a current career or career-conditional employee of NIH at the GS-5 level or above or wage-grade equivalent or on any other type of appointment that offers noncompetitive conversion during the application period.

This year's program closes on Mar. 13. Interested applicants should review the MI web site at <http://internships.info.nih.gov>.

To find out more about the MI program, attend one of the information sessions: 3/1, 3/3 or 3/7. No reservations are necessary.

Individuals with disabilities who need sign language interpreters or other accommodation to participate in the information sessions should contact Sharon Ballard at (301) 496-0264 or the Federal Relay (1-800-877-8339).



### Former NIEHS Student Worker Zhou Named 2005 Davidson Fellow

A 16-year-old high school student who spent the summer of 2004 at NIEHS was named a 2005 Davidson Fellow. The award carries a \$25,000 scholarship. John Zhou of Northville, Mich., won the science award for his project, "A Study of Possible Interactions Among Rev1, Rev3 and Rev7 Proteins from *Saccharomyces Cerevisiae*."

His project used yeast cells to study the role of proteins in DNA with results that suggest a new molecular model for proliferating cell nuclear antigen (PCNA) of translesion DNA replication, according to the Davidson Fellow web page. His research indicates the same molecules that have the ability to let the DNA replication process occur may also be a source of mutations. The results of his study not only impressed the contest judges, but also will help scientists learn to enhance or suppress the function of these molecules, which is important in a wide variety of cancer treatments.

Zhou was a special volunteer in Tom Kunkel's lab, the Laboratory of Structural Biology, under the supervision of Sean Zhong. During the 5 weeks he worked at NIEHS during the summer between his sophomore and junior years in high school, he conducted hands-on lab research related to DNA replication fidelity, learning technical procedures such as PCR, electrophoresis and restriction enzyme digestion.

Zhou said Kunkel, Zhong and the other lab members taught him the ropes of their research, showed him lab techniques and taught him how to use equipment, all the while making him feel at home. "As a result of the exposure to molecular biology and the expert guidance from NIEHS, I have developed a keen interest towards the biomedical sciences and plan to pursue that area at Harvard, where I will most likely be attending next year. The laboratory skills and research fundamentals at NIEHS have been a tremendous factor in the other research that I have pursued in the past year and will continue to be important in college and beyond," Zhou said by email.

The whiz kid hopes to work at NIH again to continue building his knowledge and skills in biology. That interest, he said, has "already been fostered so thoroughly by the NIEHS experience."—Colleen Chandler



### Heart Disease Risk Factors Study for African Americans

Healthy volunteers are needed for a study investigating the relationship of obesity to heart disease risk factors in healthy, non-diabetic African-American men and pre-menopausal women between ages 18-49. Specifically, the study is looking at risk factors for triglyceride concentration and the triglyceride-related risk factors of unhealthy cholesterol (low-density lipoprotein) and body fat distribution. There will be a series of four outpatient visits to the Clinical Center, in which participants will have body fat analyses, EKG, blood tests including cholesterol profiles, an oral glucose tolerance test, resting energy expenditure and an intravenous glucose tolerance test. Compensation provided. Call (301) 402-7119 for information. Refer to protocol 99-DK-0002.

### Can Chocolate Help Your Health?

The National Center for Complementary and Alternative Medicine seeks volunteers to participate in a 6-week study evaluating the effect of dark chocolate on blood pressure and the blood's glucose and insulin levels. Participants will help researchers learn more about chocolate's impact on hypertension and diabetes. Participants will be asked to take dark chocolate and a placebo (inactive treatment). To participate, you must be: persons with hypertension (high blood pressure) who can be safely taken off anti-hypertensive medications; age 21 to 65; not taking other medications or nutritional supplements for any illnesses besides hypertension or high cholesterol. Compensation and dark chocolate will be provided. For more information, call (301) 496-3244.

### Healthy Volunteers Needed

Doctors at NIH are conducting a study that examines the tongue. Call 1-866-444-2214, (TTY 1-866-411-1010). Refer to study 01-CC-0044. Compensation is provided.

### Siblings with JRA

Siblings with juvenile rheumatoid arthritis (JRA) are invited to participate in NIH study 03-E-0099. Compensation provided. Call 1-866-444-2214 (TTY 1-866-411-1010).

### Men and Women Needed

Men and women ages 55-65 are needed to participate in a study of alcohol metabolism and responses. Study participation includes one 3-hour screening visit and two 8-hour study visits. Participants must be social drinkers in good health. Compensation will be provided for time and participation. If interested contact Nina at (301) 451-0308 or email ETOHSTUDY-L@mail.nih.gov.

### Caucasian Women Needed

NIMH is seeking healthy Caucasian women, ages 30-50, to match with female family members who have participated in a 1-day genetic study of schizophrenia. Protocol procedures include a blood draw, an interview, neuroimaging and neurocognitive testing. English must be a participant's native language. No overnight stays. Compensation provided. For details call (301) 435-8970 (TTY 1-866-411-1010) or email Thorpek@mail.nih.gov.

### Siblings with Myositis

Siblings with myositis are invited to participate in NIH study 03-E-0099. Compensation provided. Call 1-866-444-2214 (TTY 1-866-411-1010).



*Dr. Michael Gottesman (l), NIH deputy director for intramural research, and Dr. Richard Wyatt, executive director, Office of Intramural Research, exult with attendees at the AAALAC recognition reception.*

### NIH Intramural Animal Program Accredited

The NIH Intramural Animal Program was notified recently that it was awarded "continued full accreditation" based on a July 2005 review by site visitors from the Association for Assessment and Accreditation of Laboratory Animal Care International. AAALAC is a private nonprofit organization that promotes the humane treatment of animals used for scientific research purposes through a voluntary accreditation program.

NIH was first site-visited in 1991 and has continuously maintained AAALAC accreditation for nearly 15 years. For a program to be accredited, it must conform to the principles outlined in the *Guide for the Care and Use of Laboratory Animals* (National Research Council, 1996). This site visit is similar to the Joint Commission on Accreditation of Healthcare Organizations review of the patient care program provided in the Clinical Center.

The Bethesda and Poolesville animal facilities comprise the largest single site for laboratory-related animal facilities in the world (545 animal rooms totaling nearly 700,000 square feet). Due to the scope and magnitude of the intramural animal program, a team of 12 experts from academia, government and the biomedical industry, representing domestic and international biomedical institutions on behalf of AAALAC, reviewed the NIH animal facilities and animal care and use committees for 5 days during July. They thoroughly assessed all 15 animal programs, reviewing not only the veterinary care and husbandry provided in the animal facilities but also the 1,500 animal study proposals used to prescribe how animals are used in research at NIH. They also studied support programs including occupational health, training, security and disaster planning.



*Jennifer Concannon, Mathew Tenace (c) and William Givens of Priority One work for ORS in Bldg. 10A and enjoy the reception.*

PHOTOS: JANET STEPHENS



*Younger, Sturdier Versions Needed*

## **Trademark Crab Apple Trees To Be Replaced**

If you've walked around the southeast corner of the campus in springtime, you've seen them. They look like vast umbrellas covered with pink snowballs but they're actually Arnold flowering crab apple trees, or *Malus arnoldiana*. These broad, graceful plants bracket the two NLM buildings, 38 and 38A, and are as much an NLM trademark as the funky geometric roof. Sadly, they're not in good health and will soon have to be replaced.

"The flowering crab apples are about 50 years old and that's about 10 years past their prime," explained Lynn Mueller, head of grounds maintenance at the NIH Office of Research Facilities. "You can see that just about each tree is now suffering from heartwood decay, root rot and branch dieback. Some are leaning over as a result of root failure. Like all living things, these beautiful trees have a natural life span and they've come to the end of it. Unfortunately, it's time to do something about that. It will be a tragedy removing them as they have become an NIH landmark."

The trees are an old variety not commonly grown by nurseries anymore. Over the past 40 years, however, many hardier varieties have been developed. Mueller has been scouting replacement plants at area nurseries and hopes to begin removing the current trees and planting replacements between now and late March.

"To be honest, it will take about 10 years to regain that distinctive umbrella form," Mueller pointed out. "But, in the meantime, the small trees will bloom and grow, and we'll immediately begin to prune them into that umbrella shape. We'll treat the outgoing and incoming trees with tender loving care and will do most of the work on weekends, so that we don't disturb pedestrian or vehicle traffic." —**Melanie Modlin**

PHOTOS: BILL BRANSON, FRAN SANDRIDGE, LYNN MUELLER



*The flowering crab apple trees that ring the National Library of Medicine are capable of supporting "blossom" in both spring and winter, but must soon be replaced.*