Preliminary Program for CME, October 9–10, 2003

The Office of Continuing Medical Education and the Alumni Association will present a special alumni-only CME event: "Updates and Controversies in Medicine" on October 9 and 10, 2003 on the Jefferson campus. Our preliminary agenda, showing invited faculty, is shown below.

Objectives:

- Review current practice in the treatment of cardiovascular and related diseases, women's health, diabetes, cancer screening, and prostate cancer.
- Discuss the management of specific cases to demonstrate application of current knowledge to practice-based scenarios, utilizing an audience response system.
- Analyze cases from a medico-legal perspective.
- Understand the implications of advances in genetic disease in current practice.

Jefferson Medical College of Thomas Jefferson University, as a member of the Consortium for Academic Continuing Medical Education, is accredited by the ACCME to provide continuing medical education for physicians.

Your suggestions are welcome as we develop the final agenda. Please check our website for program updates! ***http://jeffline.tju.edu/jeffcme***

Updates and Controversies in Medicine 2003
Geno Merli '75 (Course Director)

Day One, Thursday, October 9

8:30 – 8:35	Introduction of Program (Dr. Merli)
8:35 – 9:15	New Antithrombotic Drugs: Changing Paradigm of Care (Dr. Merli)
9:15 – 9:55	Update: Heart Failure Management Strategies (Dr. Feldman)
9:55 – 10:10	Questions and Answers
10:10 – 10:20	Break
10:20 – 11:00	Debate: Pros and Cons of Estrogen Replacement Therapy (Dr. Klein vs TBA)
11:00 – 11:40	Update: Where are we with cancer screening? (Dr. Wender)
11:40 – 12:00	Question and Answers
12:00 – 1:15	Lunch
1:15 – 2:15	Workshop: Medical-Legal Cases (Ms. Joann Rosenthal)
2:15 – 3:15	Workshop: Diabetes Management Strategies (Drs. Goldstein, Wender)
3:15 – 3:30	Break
3:30 – 4:30	Controversial Case Management Workshop (Drs. Menajovsky, Merli) (Audience Response Format)
4:30	Adjourn

Day Two, Friday, October 10

8:30 – 8:35	Introduction
8:35 – 9:15	Update: Management of Prostate Cancer (Dr. Gommella)
9:15 – 9:55	Controversy: Do all patients require cardiac evaluation prior to non-cardiac surgery? (Dr. Weitz)
9:55 – 10:10	Questions and Answers
10:10 – 10:30	Break
10:30 – 11:10	Update: Genetic diseases: What have we learned and how do we use the information? (Dr. McKenzie)
11:10 – 11:50	Newly approved medications: Are they innovations in the management of diseases? (Dr. C. Cheng)
11:50 – 12:00	Questions and Answers
12:00	Adjourn

Events This Fall

August 8, Friday
Jefferson Medical College Opening Exercises and White Coat Ceremony for entering students, 9:30 until 11:30, Scott Plaza: Alumni are urged to participate! The Alumni Association has donated the white coats which symbolize the rite of becoming a physician.
Freshman Family Welcome, Jefferson Alumni Hall, Eakins Lounge

September 25, Thursday
Alumni Executive Committee, Jefferson Alumni Hall, Faculty Club

Alumni Weekend, October 9–11

October 9–10, Thursday all day and Friday morning, CME program – see schedule at left
October 10, Friday, 6:00 P.M., Alumni Banquet, Jefferson Alumni Hall
October 11, Saturday, Clinic Presentations, Women's Forum, Dean's Luncheon, Reunion Parties as follows:

1943	60th	Jefferson Alumni Hall – Faculty Club West
1948	55th	Jefferson Alumni Hall – Eakins Lounge
1953	50th	Union League – Marble Room
1958	45th	Ritz-Carlton – Plaza
1963	40th	Philadelphia Club
1968	35th	Park Hyatt – Cliveden Room
1973	30th	Union League – McMichael Room
1978	25th	Ritz-Carlton – Pavilion
1983	20th	Park Hyatt – Conservatory
1988	15th	Park Hyatt – State Drawing Room
1993	10th	Jefferson Alumni Hall – Dining Room
1998	5th	Jefferson Alumni Hall – Faculty Club East
Postgraduate Alumni – Jefferson Alumni Hall – Cafeteria		

October 24, Friday
President's Club Annual Dinner, The Crystal Tea Room, Wanamaker Building, Philadelphia

December 3, Wednesday
Career Day I for sophomore/junior students, Jefferson Alumni Hall

December 4, Thursday
Career Day II for sophomore/junior students, Jefferson Alumni Hall
Alumni Executive Committee, Jefferson Alumni Hall, Faculty Club

January 21, 2004, Wednesday
Freshman Beef and Brew Social, Jefferson Alumni Hall, Eakins Lounge

October 2004: Alumni Weekend '04

October 2005: Alumni Weekend '05

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June 2003
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On the front cover: ***Jack and Vickie Farber and Samuel Gandy III MD PhD at Jefferson's new Farber Institute (see page 7).***

On the back cover: ***volunteer faculty in the Doctor in Health and Illness course for first year medical students (see page 20).***

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Spring on the campus finds us preparing, with great anticipation, for the graduation of our seniors, and the promotion of each class to the next level. This event fills us all with the mixed emotions of happiness at goals well met, coupled with the sadness of separation from such a wonderful group of soon-to-be young physicians. (The Match results are on page 28 of this issue.) It emphasizes the rejuvenation of the profession, and our call to the service of the public. It also provides us with the opportunity to re-examine our educational philosophies and processes, with an eye towards continuously improving our educational programs.

Let me be clear about what I mean by continuously improving educational programs. Continuous improvement implies more than updating of information to maintain a state of currency. It means more than scrutiny of our evaluation methodologies to assure that they are fair, and measure the desired educational outcomes. In today's environment, I believe that continuous quality improvement in education requires us to challenge strongly held biases about educational processes, and look critically at our desired educational outcomes.

Many have described our health care system as broken. Others, looking from a slightly different perspective, have observed that the system is designed perfectly to produce the outcomes we observe. So, too, the observation that evaluation drives behavior and learning must be taken into account in this regard.

So it is, I believe, with our educational system. It has long been observed that physicians are not as effective communicators as they need to be. It has also been observed that physicians are not effective members of teams, and their narrow focus and staunch individualism limits their ability to function within emerging systems of care delivery. While the care of many chronic illnesses is best accomplished in teams composed of physicians of many disciplines and participants from other professions, our physicians are evaluated during their formative years based on how they function individually. Further, since competition continues to exist for positions at each successive level, team building among colleagues continues to encounter the barrier of self-interest. Finally, the paradigm of the physician as the sole omniscient repository of all knowledge medical is challenged by both the massive explosion of medical information, as well as the ubiquity of information directly available to patients on the internet. Yet, we continue to evaluate medical students, and drive their knowledge, behaviors and skills with education and evaluation processes and content that rewards the behaviors we observe.

I believe that the educational system is perfectly designed to produce physicians who act in the fashion that we observe. Certainly there are "post-translational modifications" of physician behavior that occur after entry into the real world of practice. But certainly, the coping skills we (the faculty) model for them, and the basic skill set and view of the world we provide to them is the base from which that modification occurs. Further, I believe that we will not accomplish the modifications in the health care delivery system required to meet society's future needs until or unless the medical education system, and its flagships—the 125 U.S. medical schools—lead the way.

The Association of American Medical Colleges (AAMC), under the direction of Jordan Cohen MD, and the Accreditation Council for Graduate Medical Education (ACGME), under the direction of David Leach MD, have provided the first building blocks in the drive towards fundamental modification of our medical education system. The Medical School Objectives Program (MSOP), and the ACGME Outcomes Project have provided a platform for medical educators to begin to structure educational programs and evaluation methodologies based not on what we teach (content and process), but on what we expect our students to demonstrate that they know and can apply (demonstrated outcomes). This may appear initially as a semantic difference, but it clearly is a fundamental shift in educational program and evaluation design. The ACGME is beginning to discuss the linkage of resident outcomes with clinical outcomes in patients in their sponsoring teaching institutions. The concept that excellent education occurs in the setting of excellent patient care is not one that is foreign to Jefferson. It was a core value in the creation of Jefferson nearly 180 years ago.

The second major influence on the redesign of our educational programs must be the thrust towards a "zero tolerance for error" mentality for the health care system which has emerged in the public and political domain during the 1990s. This movement was accelerated in response to the Institute of Medicine's "To Err Is Human" and "Crossing the Quality Chasm" reports. The mantra of zero tolerance for error also runs through the medical liability insurance discussions ongoing in this, and other states.

The third trend is occurring in all our teaching hospitals and related teaching practices. As predicted in the late 1980s, our major teaching hospitals are becoming large critical care units, with very short lengths of stay and very rapid pace. There is little opportunity for the novice to learn the basics of patient interaction and care, or for the more senior resident to learn the nuances of sophisticated specialty care or procedures. Of equal concern is the rapid pace, and business practice conscious behavior required in the ambulatory arena. Many thoughtful, interested teachers have been unable to keep up with the conflicting demands of education and financially prudent practice in the ambulatory arena. Thus, the belief that we can just "shift education" to the ambulatory arena as a solution to inpatient constraints appears unrealized.

The best summary of the fundamental shift in physician skill set required that I have seen was provided during the Raymond C. Grandon ('45) Lecture on May 8 of this year, by Kenneth Shine MD, President Emeritus of the Institute of Medicine, and Director of the RAND Center for Domestic and International Health Security. In his provocative presentation, he challenged the audience to closely review the behaviors valued in our physician workforce in the mid to late 20th century. He posits that the changes needed to bring about positive outcomes in patient care demanded in the current and emerging environment will require significant changes in systems of care, and the physicians who function within these systems.

Importantly, many of the values that we have attempted to inculcate in the past 25 years are durable, important, and should not be

changed, but rather strengthened. These include the timeless commitment to each individual patient under their care, the altruistic approach to the needs of one's patients, the absolute requirement for honesty, integrity, truth telling, excellence, compassion, and respect. These values are the core of our profession and its contract with society, and must be durable and expanded in any revision of educational processes or outcomes. I propose, however, that certain of the values which we have inculcated in our students, residents, and fellows over the past quarter century in the "unwritten curriculum" are in need of revision. These values were: autonomy in the extreme; continuous knowledge accumulation from the perspective of the physician as the omniscient and sole repository of all knowledge medical; nurturing a culture of blame, shame, and secrecy for mistakes or for failure to recall memorized information; and minimization of the importance of others, including the systems of provision of care, in the care of our patients.

Contrast this with the physician skill set which Dr. Shine believes is required in the 21st century. These skills are: teamwork, and the ability to not only lead, but also be a member of a team; the ability to work effectively with other professionals; the ability to move beyond personal knowledge accumulation to commitment to continuous change and improvement of personal skills as well as the systems of care within which we function; the ability to gain personal gratification not only from individual performance, but also that of the care teams in which health professionals function; the ability to function as a partner with patients and family in their quest for patient centered health care; the orientation towards advocacy with, and on behalf of patients and their needs; and finally the recognition that all relevant information cannot be memorized, and that skills in management of information (and use of those skills) are essential to delivery of evidence based care.

Physicians must be the leaders of the evolution of health care delivery systems. They must, however, work effectively at every level in complex systems to achieve this position of leadership. Our core values are pivotal in structuring and leading complex (as opposed to complicated) systems. Those values must remain those to which the profession has committed since Hippocrates: altruism, respect, compassion, integrity, honesty, truth telling, and commitment to excellence. Stewardship of resources is an essential addition to this list, in order to assure that all Americans have access to core health services.

At Jefferson, we continuously review, enhance, and improve our educational and evaluation systems, and commit that these values will underpin our efforts. Indeed, these are our institutional values, the preamble to our strategic plan, and the core values of professionalism. They are essential as we move to a "future oriented" curriculum—protecting the best of our past, while embracing the challenge of change for the future.

Thomas J. Nasca '75
Senior Vice President, Thomas Jefferson University
Dean, Jefferson Medical College
President, Jefferson University Physicians

Update on Transplant Surgery

In July 2000, Donald Dafoe MD was named the Samuel D. Gross Professor and Chairman of Surgery. Dr. Dafoe's expertise lies in transplantation, and he was formerly chief of the transplantation program at Stanford University Medical Center in California where he built the program in abdominal organ transplantation from zero activity to more than 225 transplants a year.

At Jefferson, Dr. Dafoe has been particularly busy working with Arthur Feldman MD, Chairman of the Department of Medicine, to build a new program in heart failure and cardiac transplantation. "We have recruited faculty for each other and expect to announce the new head of cardiac surgery very soon," Dafoe reports.

In addition to administering the Department of Surgery, Dr. Dafoe is actively involved in teaching at Jefferson. It is evident that he enjoys mentoring when one observes him on rounds with residents. He explains that he was lucky to have an excellent mentor when he was training at Penn. Dr. Dafoe's father was a surgeon, so he was programmed to go into surgery, and it was a field he liked, but it wasn't until he met Clyde Barker MD, former Chairman of Surgery at the University of Pennsylvania, that he became interested in academia. "He was very charismatic and got me fired up about going into academics, particularly transplantation," he recalled. "Up until then, my plan was to do training and go back to rejoin my father in Appleton, Wisconsin. But I found transplantation to be so exciting at the time, and I knew it would get better. It was the late 1970s, and the results weren't particularly good. But they were having some stunning success, and I knew that during my career it would get better and better, and it has."

Transplantation has evolved more rapidly than some other medical fields. Dr. Dafoe recalls some 20 years ago when the field was relatively young. "We were going up against a major evolutionary barrier, which is allografting. There was a big hurdle to get by. Then, I think we just hit a point in the understanding of cellular biology and immunology. That, and some very effective drugs came along which changed things by getting rejection under control, and some very persistent transplant surgeons helped on the technical side developing the field. A lot of things seemed to align well both scientifically and clinically to push the field forward. It was a field developed mostly by surgeons, which I am proud of. Surgeons were the leaders who brought transplantation to fruition."

Today, Dr. Dafoe said, the problems for patients involved in transplantation have shifted away from the acute rejection of former years. Acute rejection now occurs in only about 15 percent of patients. The biggest concern today is to get patients off anti-rejection drugs because they all have negative side effects. "Secondly," he states, "there's something called 'chronic rejection' which is a day-to-day slow wearing away attack on the graft, which is still a problem. So, the main hurdles today are chronic rejection, the organ shortage, and the fact that the patient still needs long term drugs. These are the Holy Grails now."

Through research Dr. Dafoe believes these problems will be addressed in the coming decades. He is particularly hopeful in the areas of

continued on page 30

The New Jefferson Hospital for Neuroscience

The newly created Jefferson Hospital for Neuroscience now occupies the former Wills Eye Hospital building at Ninth and Walnut Streets in Center City, adjacent to the Bluemle Life Sciences Building. This facility, dedicated to neurology and neurosurgery, enables Jefferson to meet the increasing demand for treatment in this area.

Major changes in the JHN physical layout coincide with the appointment of Abdolmohamad Rostami MD PhD as Professor and Chair of the Department of Neurology.

In December 2002 designs were finalized to accommodate JHN's present staff and resources, as well as to allow new space for as many as 12 researchers who will join Dr. Rostami over the months ahead.

John A. Monnier, Senior Associate Dean for Operations at Jefferson Medical College, reports, "Major interior renovation and new construction on the second and third floors is underway to house the Department of Neurology. The third floor is being almost entirely rebuilt to accommodate research laboratories and faculty. The second floor will need significant work to provide physician offices and outpatient facilities." Target date for completing all work on the second and third floors is December 2003.

The Farber Institute for Neurosciences, on the building's fourth floor, is directed by Samuel E. Gandy III MD PhD, Professor of Neurology (pictured on the cover of this issue).

The Department of Neurology's outpatient offices will be relocated from their present sites to new quarters on the refurbished second floor of JHN. These include the headache, epilepsy, multiple sclerosis, and stroke centers, among other services.

Staff and outpatient offices of the Department of Neurosurgery remain across the street at 909 Walnut Street.

A very visible piece of the consolidation is the building of a pedestrian bridge connecting the JHN building with the Bluemle Life Sciences Building. It will facilitate collaboration between researchers working in the two structures.

The consolidation project will leave intact several existing areas, including Jefferson's Geriatric Psychiatry Program on the eighth floor of JHN, inpatient beds on the seventh and sixth floors, and operating rooms on the fifth. Remaining on the street floor are the Wills Eye Hospital Emergency Department and services including admissions, food, environmental, medical records, and pharmacy.

The JHN staff has established world-class standards for the safe, effective treatment of brain tumors, brain aneurysms, stroke, epilepsy, Parkinson's disease, chronic pain, and other neurological disorders.

The neurosurgical programs are led by William A. Buchheit MD, Professor and Chairman of the Department of Neurosurgery.

Some JHN Achievements:

- JHN utilizes endovascular surgery for more patients with neurovascular disorders than any other institution in the Delaware Valley. A new procedure using a coil to treat aneurysms has received much publicity. JHN's Chief of Cerebrovascular Surgery, Robert H. Rosenwasser MD (see page 10), was one of the nation's first neurosurgeons to perform this and other procedures to treat brain aneurysms, stroke, arteriovenous malformations, and carotid artery disease, reducing the need to open the skull. His associate, cerebrovascular and interventional neurosurgeon Ronald Benitez MD, is also skilled in these techniques.

- JHN was the first facility in the world to have both a linear accelerator designed for and dedicated to radiosurgery, as well as a gamma knife, for nonsurgical treatment of brain tumors and epilepsy. Radiosurgery innovator David W. Andrews MD directs the Division of Stereotactic Radiosurgery. More tumors are treated here than at any other institution in the region.

- Jefferson's Epilepsy Center is the largest in the Delaware Valley. Michael R. Sperling MD, the center's Director, Michael J. O'Connor MD, Director of Surgical Epilepsy, and his new associate, Ashwini D. Sharan MD, lead a team of neurosurgeons, neurologists, and neuropsychologists, working closely with radiologists and other specialists.

- JHN is one of the few centers in the nation which performs a spinal cord stimulation implant for management of chronic pain. Giancarlo Barolat MD, Director of the Neuro-Implant Program, and an internationally recognized pioneer of surgical neuroimplantation techniques, receives patient referrals from all over the United States.

- JHN can now offer deep brain stimulation for patients with Parkinson's disease, essential tremor, or dystonia. Neurosurgeon Ashwini D. Sharan MD (see page 10) is experienced in this neuroimplantation surgery that has proven to be a safe, painless, and highly effective restorative of patients' mobility and independence.

- More JHN neurosurgeons appear on *Philadelphia Magazine*'s "Top Docs 2002" than any other facility's.

In addition to these activities of the JHN team of neurosurgeons, Thomas Jefferson University Hospital neurosurgeons, including James Harrop '95, continue as leaders in complex spinal procedures for spinal cord injury.

"No facility is better staffed or equipped to offer the extraordinary results that make contemporary neurosurgery so exciting than the Jefferson Hospital for Neuroscience," concludes Dr. Buchheit.

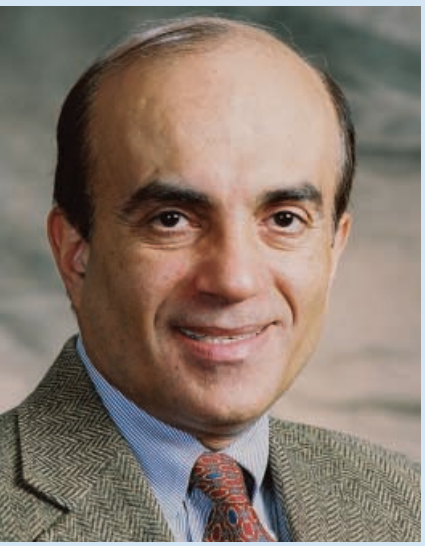
Robert Neroni

Rostami Appointed Chair of Neurology

Abdolmohamad Rostami MD PhD has been named Professor and Chair of the Department of Neurology. Previously he was Director of the Comprehensive Multiple Sclerosis Center, Chief of the Division of Multiple Sclerosis and Neuroimmunology, and Director of the Penn Center of Excellence for Autoimmune Diseases at the Hospital of the University of Pennsylvania.

He has served as a tenured Professor of Neurology and of Medicine at the University of Pennsylvania and is an Adjunct Professor at the Wistar Institute, Philadelphia. "Dr. Rostami's research and clinical expertise will bring added depth and breadth to our neuroscience research program, a major initiative at Jefferson," said Thomas J. Nasca '75, Dean of Jefferson Medical College.

Dr. Rostami will work closely with the members of the Farber Institute for Neurosciences at Thomas Jefferson University to enhance programs for patients with neurodegenerative diseases, and work with Jefferson's faculty to build upon existing programs for patients with cerebrovascular disease and stroke, epilepsy and seizure disorders, and headache.



Dr. Rostami currently is the program director of two program projects and the principal investigator of RO1 grants being funded by more than $13 million in grants from the National Institutes of Health (NIH), supporting extensive research in multiple sclerosis and neuroimmunology. He is also funded by the National Multiple Sclerosis Society and is investigator for several clinical trials of new treatments for the disease. Rostami is the author of more than 100 scientific papers.

Dr. Rostami is the recipient of the Special Recognition Award from the Guillain-Barré Syndrome Foundation International, as well as the Outstanding Service Award and the Outstanding Leadership Award from the National Multiple Sclerosis Society. He also received an honorary master of arts degree from the University of Pennsylvania in 1992.

A fellow of the American Academy of Neurology and the Royal Society of Medicine in London, he is a member of the American Neurological Association, the International Society of Neuroimmunology, the International Society of Neuroimmunomodulation, the International Brain Research Organization, the International Union of Immunological Societies, the American Association of Immunologists, and the Society for Neuroscience.

He has chaired the medical advisory board of the National Multiple Sclerosis Society, Delaware Valley Chapter, and is a member of its board of trustees. He is also on the medical advisory board for the Guillain-Barré Syndrome Foundation International, and has served on various study sections of the National Institutes of Health.

The new neurology chair currently serves as Deputy Editor-in-Chief of *Multiple Sclerosis* and as an editorial board member of the *Journal of Neurological Sciences*, the *Journal of Clinical Neuromuscular Disease,* and *Experimental and Molecular Pathology*.

Farber Institute Opens Its Doors

The Farber Institute for Neurosciences on the fourth floor of the Jefferson Hospital for Neuroscience was formally dedicated on May 19, at a ceremony that included speeches by two well known public advocates for Alzheimer's disease research: Patti Davis, daughter of former President and Mrs. Ronald Reagan, and actor David Hyde Pierce of TV's "Frasier."

Nobel laureate and neurobiologist Paul Greengard MD, Professor and head of the Laboratory of Molecular and Cellular Neuroscience at the Rockefeller University, was an honored guest. Dr. Greengard chairs the Farber Institute's External Scientific Advisory Board. He and his colleagues received the Nobel Prize in 2000 for their discovery of how dopamine and a number of other transmitters in the brain exert their action in the nervous system.

The Farber Institute is a multidisciplinary center initially focusing its efforts on basic and clinical research in Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), and other neurodegenerative disorders.

"This kind of institute, dedicated to researching Alzheimer's and related illnesses, is needed in order to work in the best interests of the increasing number of patients affected by these debilitating illnesses," said Samuel E. Gandy III MD PhD, Professor of Neurology and of Biochemistry and Molecular Pharmacology, and Director of the Farber Institute.

In December 2001, the Farber Family Foundation, Incorporated announced a gift of $10 million to Thomas Jefferson University to establish this new institute. It was one of the largest gifts the university has ever received. Jack Farber, President of the foundation, and Chairman of the Board of CSS Industries of Philadelphia, and his wife Vickie have been touched personally by neurodegenerative diseases. Mrs. Farber's father died from ALS; her mother died with Alzheimer's disease.

Mr. Farber has been a member of Thomas Jefferson University's Board of Trustees since 1984, and was Chairman of the Board from January 1995 to June 2000.

The Farbers are pictured with Dr. Gandy on the cover of this issue.

The Farber Institute is pursuing new treatment modalities and recently inaugurated its participation in the first clinical trial in North America aimed at the protein that accumulates in the Alzheimer brain.

Researchers Show That Human Neural Stem Cells Can Become Dopamine-Making Brain Cells in the Laboratory

Biologists at the Farber Institute for Neurosciences have shown for the first time that in the laboratory they can convert some adult human neural stem cells to brain cells that are capable of producing dopamine, the brain chemical missing in Parkinson's disease. If the researchers can better understand the process and harness this ability, the work may someday lead to new strategies in treating neurodegenerative diseases such as Parkinson's.

Developmental biologist Lorraine Iacovitti PhD, Professor of Neurology and Associate Director of the Farber Institute, is searching for ways to convert stem cells into dopamine-making neurons to replace those lost in Parkinson's. In previous work, she and her co-workers showed that mouse neural stem cells placed in rats with Parkinson's disease could develop into brain cells that produced tyrosine hydroxylase (TH), the enzyme needed to make dopamine.

Dr. Iacovitti wanted to see if human neural stem cells could become dopamine-producing brain cells as well. She and her colleagues grew neural stem cells in a laboratory dish. Using a cocktail of protein growth factors and nutrients, the researchers found they could coax approximately 25 percent of the stem cells to make TH in the dish, proving the stem cells had the capacity to manufacture dopamine. What's more, when they removed the growth factor cocktail, the cells continued to produce the enzyme.

She reported her team's findings in November at the annual meeting of the Society of Neuroscience.

"We have two examples of human stem cells that do this," she says. "The obvious extension [of these results] is to take those predifferentiated human dopamine neurons and transplant them into Parkinson's disease model systems."

But first, Dr. Iacovitti would like to purify these neurons. Her group has developed ways of tagging live dopamine neurons with a fluorescent marker, she says, "enabling us for the first time to purify or enrich the number of dopaminergic neurons and transplant them into Parkinsonian animal models."

Ultimately, she says, they hope to develop this as a treatment for Parkinson's disease in people.

Scientists Find Evidence of Greater Sensitivity to Addictive Drugs in Adolescence

Researchers at Jefferson have evidence in animals that the young, adolescent brain may be more sensitive to addictive drugs such as cocaine and amphetamines than either the adult or newborn. The work may help lead to a better understanding of how the adolescent human brain adapts to such drugs, and provide clues to changes in the brain that occur during drug addiction.

Scientists led by Michelle Ehrlich MD, Professor of Neurology and a member of the Farber Institute for Neurosciences, and Ellen Unterwald PhD, Associate Professor of Pharmacology at Temple University School of Medicine, found a greater increase in a certain protein in the region of the adolescent mouse brain called the striatum, following chronic exposure to drugs such as amphetamine and cocaine, than they did in either very young mice or adults.

Such psychostimulant drugs affect the brain's striatum in different ways, potentially affecting both movement and locomotion, or the "reward" system. This "molecular adaptation," says Dr. Ehrlich, could be significant. "An increase in this protein may be important because it could also affect other molecules that could lead to long-lasting changes in the brain in response to psychostimulant drugs." The protein, called Delta FosB, is a transcription factor and plays a role in regulating gene expression. Earlier research by other scientists had shown increased amounts of Delta FosB in adult brains following chronic exposure to psychostimulants.

The team, which included scientists at the Nathan Kline Institute in Orangeburg, New York, reported its findings November 1 in the *Journal of Neuroscience*.

"Periadolescence and adolescence are when addiction usually begins, so we will be looking to see if this increase is a clue to sensitivity to addiction, and sensitivity to such drugs as therapeutic agents," says Dr. Ehrlich. "Many molecules have been implicated in both therapeutic and addictive responses to psychostimulants," she notes.

Dr. Ehrlich's team examined how the mice responded to cocaine and amphetamine. They looked at the effects of the drugs on Delta FosB in three different age groups: post-weanling, or day 22; adolescent, days 33-43; and adult, or about six weeks of age. Each group was given cocaine, amphetamine, or saline.

They found that in the adult, Delta FosB was increased in the caudate nucleus, part of the striatum associated with motor activity, particularly hyperactivity and attention deficit syndrome. They did not see similar increases in the accumbens, another part of the striatum that is associated with reward from psychostimulants. In the post-weanling mice, there was an increased response in the caudate only to amphetamine.

When they looked at the adolescent mice, they found Delta FosB was made in increased amounts in both areas of the brain in response to the drugs.

"The implications are that there is an increased adaptation in the younger brain than in the older brain to these psychostimulants," she says.

The results raise several questions. "What are the behavioral

correlates of the increase in protein activity?" asks Dr. Ehrlich. "Does this make them more prone to self-administer psychostimulants, meaning these mice could be a model of addiction? Does this make them more prone to hyperactivity? Are they more tolerant of higher doses of medication? These questions are relevant to addiction and to therapeutic use of these medications in these age groups."

Dr. Ehrlich and her co-workers have begun looking at the causes of such adaptations in the brain. They are studying some of the specific molecules involved in new mouse models. "At this point, many of the drugs that are being used therapeutically and in the treatment of addiction are being targeted to very restricted molecules," she says. "The question is, would they be better targeted to other molecules?"

Testing a New Stroke Prevention Drug

Neuroscientists at the Farber Institute will help conduct the first clinical trial looking at the potential usefulness of a drug to prevent patients who have already suffered a hemorrhagic, or bleeding stroke, from having a second one. The Phase II trial, led by Barry Rovner '80, Director of Clinical Alzheimer's Research at the Farber Institute, Samuel Gandy III MD PhD, Professor of Neurology and Institute Director, and Rodney D. Bell MD, Medical Director of the Acute Stroke Center and Professor of Neurology and Neurosurgery, will test the biological properties, activity, and safety of a drug, NC-758, in patients with a disease called cerebral amyloid angiopathy (CAA).

Dr. Rovner and his colleagues hope the trial will enable them to determine whether or not NC-758 warrants further testing in a larger trial. They also would like the trial to provide ideas of potentially effective doses and schedules for patients.

In CAA, amyloid, a normal protein, accumulates in blood vessel walls in the brain, weakening them and leading to stroke. Medicines such as NC-758 have been shown in laboratory studies to block the accumulation of amyloid in such vessels.

Alzheimer's disease is characterized by an excessive buildup of amyloid in the brain. Alzheimer's patients who develop amyloid angiopathy have an increased rate of stroke, notes Dr. Rovner. "If the drug shows effects on CAA, it could potentially help patients with Alzheimer's," he says.

"This is the first clinical effort against CAA, a major cause of bleeding strokes in the elderly and a condition that is more common than previously thought," he says. "Approximately 30 of every 100,000 Americans 65 or older will develop a brain hemorrhage from CAA.

Even more importantly, "It's the first clinical trial in North America aimed at the protein that accumulates in the brains of Alzheimer's patients," notes Dr. Gandy.

The trial will involve patients at multiple centers who have suffered a hemorrhagic stroke, also known as a cerebral hemorrhage. In the current study, patients will receive NC-758 for 12 weeks.

While most such strokes are not fatal the first time, they are a frequent cause of disability and are often followed by a second stroke. Dr. Rovner notes that the role of CAA as an underlying cause of disease, including hemorrhagic stroke, has become more widely recognized in only the last several years. The trial is being funded by a grant from the National Institutes of Health and is based at Massachusetts General Hospital.

Rovner Heads Clinical Alzheimer's Research

Neuropsychiatrist Barry W. Rovner '80, who continues as Director of the Division of Geriatric Psychiatry, and Professor of Psychiatry and Human Behavior, has been named Director of Clinical Alzheimer's Research at Jefferson's Farber Institute for Neurosciences.

Under the guidance of Dr. Rovner, the Farber Institute in collaboration with the Geriatric Psychiatry Program now provides Alzheimer's evaluations that include comprehensive and individualized diagnostic services, therapeutic options to patients with various types of dementia, and support and educational services to patients' family members. Alzheimer's disease affects four million people in the United States over the age of 65.

Recently, at Jefferson, Dr. Rovner has also been directing a clinical trial studying the link between depression and vision problems in the elderly. Through a $2.4 million National Institute of Mental Health grant, he is conducting a five year, randomized clinical trial on depression and age related macular degeneration. AMD, the most common cause of impaired vision, has no cure, and over time affects sight in both eyes. Causing a blind spot in central vision where visual acuity is the sharpest, AMD severely curtails the ability to handle basic activities of daily living and often leads to depression.

Dr. Rovner's group is enhancing patients' problem solving skills to prevent depression and enable them to function at their highest levels. "This research has direct implications for helping patients with Alzheimer's disease and their families as well," he said.

Earlier in his career, Dr. Rovner was Associate Professor of Psychiatry and Behavioral Sciences at Johns Hopkins University School of Medicine, where he was active in Alzheimer's research. His training had been at Hopkins, where he was a neuropsychiatry fellow in the dementia research clinic from 1984 to 1985 and was also the Chief Resident in psychiatry from 1983 to 1984. The International Psychogeriatric Association awarded Rovner its first prize for his research on mental disorders in nursing homes in 1989. He has more than 100 publications.

New Hope for Patients with Late Stage Parkinson's Disease

Neurosurgeons at Jefferson now have an alternative way to treat Parkinson's disease by supplying controlled electrical signals through electrodes implanted deep within the brain. This surgical procedure, called Deep Brain Stimulation (DBS), is for those patients whose disease has stopped responding to drug treatment.

"We're essentially putting electrodes inside different areas of the brain and trying to re-establish the brain's disordered circuitry in Parkinson's disease," says Ashwini D. Sharan MD, Assistant Professor of Neurosurgery, who leads the new program. Dr. Sharan performed approximately 50 DBS surgeries when he was at the Cleveland Clinic prior to coming to Jefferson in 2001.

In addition to electrodes, doctors subsequently implant a pacemaker in the chest to regulate the electrical signals in the brain.

According to Dr. Sharan, Parkinson's disease, which is a progressive, neurodegenerative disorder, is an ideal candidate for this treatment because it involves a single area of the brain.

Medication for the illness should always be tried initially, he says. But in the next decade, 80 percent of people with Parkinson's will fail medications (usually the drug L-dopa) and have untreatable side effects. DBS has been FDA-approved for Parkinson's since February 2002 for those who failed medical treatment.

Some 1.5 million people in this country have Parkinson's disease. Less than one percent are operated upon, though about 15 percent could benefit from the surgery, according to Dr. Sharan.

Surgery to implant the DBS electrodes typically lasts six to eight hours. Recuperation time in the hospital is generally 48 to 72 hours for older patients, while younger patients may be able to go home the next day. After a week, they return as outpatients for a second day, when the pacemaker is put in. Finally, a month later, patients go back and the pacemaker is turned on.

"Patients with a lot of tremor, dyskinesia (involuntary movements), and bradykinesia (extreme slowness of movement) are the ones who respond the best to DBS surgery," he says. "Most patients' brains are working well early in their disease, so this is a major quality-of-life issue, because they know their body is not keeping up with them."

DBS, says Dr. Sharan, may have several advantages over other treatments. Its effects are very precise and controlled, and what's more, it's reversible. "If we take the electrode out of the brain, the brain is no better or worse, aside from having an incision." Patients can control their own daily treatment simply by turning the device on or off, and can adjust the current amount and frequency themselves.

How long do the effects of DBS implants last? It's variable, he says, depending on how fast the Parkinson's progresses. The first patients were implanted in 1987 and many haven't lost the effects of the treatment as yet, he notes. If the treatment becomes ineffective, it's probably because the disease is progressing.

According to Dr. Sharan, DBS controls about 70 to 80 percent of tremor, 60 to 70 percent of rigidity, and 50 to 60 percent of akinesia, or abnormally slow gait. Approximately one-half of individuals can cut their medications (L-dopa) by half. And 10 to 20 percent stop taking their medications completely.

In Parkinson's, the brain's circuitry has gone awry. A portion of the brain called the subthalamic nucleus is overactive. These cells produce glutamate, an excitatory neurotransmitter, or chemical message carrier. Another region of the brain called the substantia nigra, which is also important for the coordination of movement and where the brain chemical dopamine is made, indirectly controls the subthalamic nucleus. Parkinson's is caused by the deterioration of dopamine-producing nerve cells.

"We're hoping that by putting electrodes in the subthalamic nucleus, we can shut off the hyperactivity," he says. "The mechanism is not precisely understood right now."

While Parkinson's is by far the disease for which DBS surgery is most often used, it also has applications for treating both essential tremor and dystonia, an inherited disease in which victims suffer from spasmodic, twisting body movements.

Dr. Sharan is convinced DBS has a bright future. Within three to five years, rechargeable batteries will be available to implant in a patient's head, eliminating the second part of the surgery. Instead, he says, they'll be able to wear a cap that will recharge implants while they sleep. Rechargeable electrodes will be planted on top of their heads. Pacemakers will be able to be programmed by phone (telemetry) for those patients who live in remote areas.

Rosenwasser Elected President of Society of University Neurosurgeons

Cerebrovascular surgeon Robert H. Rosenwasser MD has been elected President of the Society of University Neurosurgeons. A Professor of Neurosurgery at Jefferson, he is world renowned for his expertise in both preventing and treating brain aneurysms that are often life-threatening. Dr. Rosenwasser does more such operations annually than any other surgeon in the country.

"This is a tremendous honor for both Dr. Rosenwasser and the Department of Neurosurgery," said William Buchheit MD, Chair of Neurosurgery at Jefferson. "It reflects Dr. Rosenwasser's exceptional achievements and high standing among his peers."

Dr. Rosenwasser directs the Division of Cerebrovascular Surgery and Interventional Neuroradiology, which employs the most comprehensive approaches to cerebrovascular disease and the treatment and prevention of stroke, including microsurgery, endovascular embolization techniques for aneurysms and arteriovenous malformations (AVMs), and stereotactic radiosurgery for brain AVMs using the region's only Gamma Knife and dedicated linear accelerator. The program treats the largest volume of aneurysms, brain AVMs, and carotid endarterectomies in the region.