



American Parkinson Disease Association

# AMERICAN PARKINSON DISEASE ASSOCIATION

SPRING 2011



**G. Frederick Wooten Jr., MD,** has been named APDA's Scientific and Medical Affairs Advisor. See page 5.

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## STAGING IS NOT IMPORTANT IN EVALUATING PARKINSON'S DISEASE

By Joseph H. Friedman, MD

Patients often ask what stage of PD that they are in. I then explain the following as to why that is not an important issue.

Staging in most diseases is important in predicting how long people will live or how well they can function. This is particularly important in cancer and heart disease. Different cancers have different systems for staging as experience has accumulated to distinguish how ominous it is to have cancer spread to local lymph nodes, or distant nodes, above the diaphragm, or below the diaphragm, in the bone marrow or not, etc. So stage 2b in one disease may have a very different prognosis than stage 2b in another form of cancer, but each will be associated with a certain chance of survival for a specified period.

This is not true for staging in PD.

The staging system we use is based on a famous paper written by Margaret Hoehn and Melvin Yahr in 1967. Their paper was the first large study of the effect of L-Dopa on disease progression. In order to assess how the disease progressed, they had to develop a system to rate the severity. It wouldn't do, for example, to say "mild," "moderate," or "severe," as the readers would want to know what they meant by these terms.

In the Hoehn-Yahr (H-Y) staging system, **stage 1.0** means that the PD is limited to one side of the body. Tremor, rigidity, reduced arm swing, and slowness are present only on one side. **Stage 2.0** refers to problems affecting both sides, although one side may be only minimally involved. I should state that there are experts who think there is no such thing as stage

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## APDA RESEARCH GRANT RECIPIENTS FIND DRUG THAT STOPS PD PROGRESSION

Wenbo Zhou, PhD, applied for and was awarded an APDA research grant, "Testing Drugs That Upregulate DJ-1 in Mouse Models of Parkinson's Disease" in 2008.

For the past three years Dr. Zhou has been working at the Universi-

ty of Colorado School of Medicine with Dr. Curt Freed, also an APDA research grant recipient, and his research has led to finding a drug that stops the progression of PD in mice. It is now being tested in humans.

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# PRESIDENT'S MESSAGE



Happy birthday, APDA!

Yes, APDA is 50 years old this year, a bitter-sweet milestone because we still do not know the cause(s) or have found the cure for the disease. We are very proud, however, of the

role we have played in funding pioneering research, providing education and support to the 1.5 million Americans with the disease, and developing the country's largest grassroots Parkinson's organization.

On the science front, APDA-funded research has led to medications and procedures that have extended and improved patients' quality of life, and continues to close in on possible causes and the ultimate cure.

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APDA's national network of awareness and fund-raising chapters, patient and caregiver Information & Referral centers, diverse support groups, and specialized national centers, is a unique resource for education, information, programs and support for every American touched by this life-altering disease.

The accompanying time line will give you a quick view of what a half century of dedication, talent, loyal support and, yes, let's not minimize hard work, has wrought. It is quite impressive, but will remain unfinished until the cure is found.

So, happy birthday, APDA – and, yes, we are accepting gifts!

Joel A. Miele Sr., PE  
President

## APDA TIME LINE

**1961:** APDA is established.

**1962–65:** APDA funds the work of Dr. George C. Cotzias, which led to establishing the effectiveness of high dose oral levodopa in treating PD and remains the standard treatment today.

**1963:** First chapter is formed on Staten Island, N.Y.

**1975:** First research grant is awarded to Cornell University – Burke Research Center, Manhattan, for \$140,000.

**1979:** First Information & Referral Center is opened at Boston University.

**Late 70s:** Support group program begins.

**1979:** George C. Cotzias, MD, Memorial Fellowship is established, a three-year (\$80,000 annually) award to assist a promising neurologist in establishing a career in research, teaching and clinical services.

**1980s:** APDA funds Dr. Roger Duvoisin research on the roles of heredity and environment in PD and his studies of patterns of inheritance in familiar cluster of the disease. Working with Drs. Lawrence Golbe, Margery Mark, William Johnson and Alice Lazzarini, he collected a number of multi-case families. One family identified as the Contursi family (named after the Italian village where it originated) was found to comprise more than 400 individuals with at least 60

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## ASK THE DOCTOR

**Q:** "I have had Parkinson's for more than 15 years. Why is it that if I take a nap in the afternoon, I feel worse than ever when I wake up? Can you explain why this is happening all the time?"

**A:** There are several reasons why a person with Parkinson's disease may awaken from a nap with worse symptoms. Which of any of these is your situation is not possible to us to determine and readers are urged not to change their treatment based on the opinions give here but the reader is encouraged to discuss what is read here with their treating physician. Depending on the length of the nap and the time since the last dose of medications, it may be that the patient's system has just run out of medications during the nap. This would be particularly common in patients taking immediate release carbidopa/levodopa especially if they have had Parkinson's disease for several years. Some patients with Parkinson's disease also may have arthritis whose symptoms sometimes can get worse with immobility and it just takes some time to "warm up."

**Q:** "I am fortunate. I have had PD for approximately eight years and the only apparent problem is my walking. Recently my walking has become significantly worse. What causes a rapid increase in walking difficulty; why wasn't it progressive?"

**A:** Problems with walking and balance are perhaps the most difficult problems to improve

with medical and the typical Deep Brain Stimulation (DBS) therapies. The fact of the matter is we don't know why use of the hands and arms improves while walking and balance may not. One possibility is that walking is an incredibly complex behavior where there are far more muscles acting over many more joints to control compared to hand and arm movements. Often treatments can help maintain good control of the upper extremities while the use of the lower extremities continues to worsen. There is reasonable evidence that DBS of the pedunculopontine nucleus (called the PPN) may be particularly helpful with walking and balance. A sudden worsening of walking or balance raises the possibility of a separate and different problem. Unfortunately, having Parkinson's disease does not protect one from having a stroke or other neurological disorders. That is why whenever there is a sudden change in symptoms it is important to have a neurologist re-evaluate the situation and not merely assume that the sudden change is due to Parkinson's disease.



**Erwin B. Montgomery Jr., MD, Sigmund Rosen, MD, Scholar in Neurology University of Alabama at Birmingham and member of APDA's Scientific Advisory Board.**

## GET PD NEWS NOW

You can receive current PD research news, helpful tips on daily living with PD, and timely notification of breaking news and alerts by subscribing to APDA's free e-newsletter. Go to [www.apdaparkinson.org](http://www.apdaparkinson.org) and click on the "Get e-updates" button on the right side of the homepage. It is free, easy and you can

unsubscribe at any time.

The Web site also includes daily news updates about Parkinson's disease from liable news media, professional publications and news releases from prestigious academic institutions.

*Materials concerning Parkinson's disease research and answers to readers' questions are solely for information and should not be used for treatment purposes, but for discussion with the patient's health care provider.*



## NEW LEVODOPA-CARBIDOPA DELIVERY SYSTEM IS IN CLINICAL TRIALS IN 18 STATES

The efficacy, safety and tolerability of a new levodopa-carbidopa intestinal gel delivery system are being evaluated in ongoing clinical trials in 18 states.

In the test process, levodopa-carbidopa is formulated as a gel and a portable pump delivers it directly into the small intestine through a tube inserted through the skin of the abdomen. The pump can be programmed to deliver the gel at an optimized rate for each individual. The aim is to overcome absorption issues and short half-life that can limit the drug's effectiveness by eliminating the time it takes for tablets taken by mouth to move from the stomach into the small intestine.

Dopamine production in the brain gradually declines in PD, and levodopa is typically helpful because it increases dopamine production and reduces the motor symptoms of tremor, rigidity, difficulty with walking, and impaired mobility. The carbidopa component has no effect on symptoms but is included to prevent side effects such as nausea

caused by levodopa.

Over time, however, many people develop fluctuations between the "on" state, during which levodopa works well, and the "off" state, when symptoms re-emerge. These fluctuations are caused by the rise and fall of drug levels that occur when tablets are taken by mouth.

The risks of the surgical procedure to insert the tube and the need to carry the pump, which can be worn in a belt bag around the waist, are potential drawbacks.

The intestinal-gel delivery system has been approved in Europe and is sold under the brand name Duodopa. If the current studies are positive, the FDA would be able to approve it for use in the United States.

*Information about the trials and which ones are enrolling participants is available at [www.Pdtrials.org](http://www.Pdtrials.org) or [www.Clinicaltrials.gov](http://www.Clinicaltrials.gov) and searching the title, "Study of Efficacy, Safety and Tolerability of Levodopa-Carbidopa Intestinal Gel in Levodopa-Responsive Parkinson's Participants."*

## APDA RESEARCH GRANT RECIPIENTS FIND DRUG THAT STOPS PD PROGRESSION

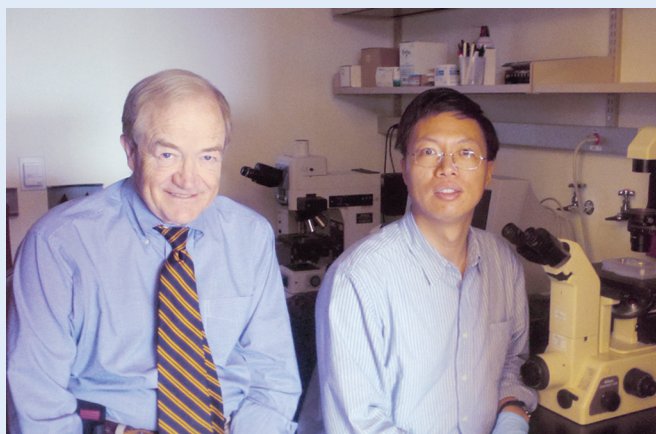
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When the brain cells that produce dopamine die, a person loses control of bodily movement. The accumulation of certain proteins has been identified as the cause of these cells' death, and the researchers found that phenylbutyrate turns on the DJ-1 gene that protects dopamine neurons by regulating oxygen and clearing out the bad protein. The drug was originally used to treat urea cycle disorders and remove ammonia from the body,

By giving phenylbutyrate to mice programmed to get PD before the disease's onset, the researchers found it could prevent the condition's development and prevent the cells from becoming abnormal and dying.

Drs. Zhou and Freed began giving phenylbutyrate

to clinical trial participants in 2009 to test its safety in people with Parkinson's and plan to publish their findings this year.



**Drs. Curt Freed and Wenbo Zhou in their University of Colorado School of Medicine laboratory.**

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## APDA TIMELINE

cases of PD in five generations. His work led to the linking of the disease to DNA markers for a small region of chromosome 4.

**1990:** First APDA Center for Advanced Research opens at Emory University, Atlanta. Currently there are nine: Emory, Boston University School of Medicine, Robert Wood Johnson Medical School; University of Virginia Medical Center, Washington University, UCLA School of Medicine, University of Pittsburgh, University of Alabama at Birmingham, University of Chicago.

**1990s:** APDA funds research at Robert Wood Johnson Medical Center, New Brunswick, N.J., which leads to the discovery of alpha-Synuclein, the protein that occurs in Lewy bodies.

**1992:** APDA establishes the country's first Information & Referral Center dedicated to the needs of young onset patients.

**1995:** APDA's Scientific Advisory Board is created from an existing Medical Advisory Board to evaluate all research grant applications. Roger Duvoisin, MD, is chairman.

**1998:** APDA co-sponsors World Parkinson Disease



Association.

**2002:** Roger C. Duvoisin, MD, Research Grant introduces a two-year (\$80,000 annually) to an established scientist to support new research.

**2005:** APDA moves into its current national headquarters.

**2007:** Research Funding reaches \$30 million mark.

**2009:** APDA establishes the first National Young Onset Center.

**2010:** APDA establishes the first National Rehabilitation Resource Center.

## APDA CELEBRATES ITS GOLDEN ANNIVERSARY THIS YEAR

APDA celebrates its golden anniversary this year. In half a century it has grown into the country's largest grassroots organization supporting scientific research and providing education and support to people with Parkinson's disease, their caregivers and families.

APDA will publish a commemorative journal as part of the yearlong celebration and invites its family across the country to participate by honoring the

life or memory of a person who has been touched by the disease. The journal will be distributed at a celebration event on Staten Island on Sept. 17, and all subscribers will receive a copy of the journal at the end of the year. A journal contract is enclosed in the newsletter, or an ad may be ordered online by visiting [www.apdaparkinson.donordrive.com/event/apdajournal.com](http://www.apdaparkinson.donordrive.com/event/apdajournal.com).

### APDA National Young Onset Center Launches Monthly e-Newsletter

Visit [www.youngparkinson.org](http://www.youngparkinson.org) and click the "Subscribe Today" link. Register and be among the first to receive important young onset news and information.

**Be Informed. Live Well. Stay Strong.**

# STAGING NOT IMPORTANT IN EVALUATING PD

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1.0, that everyone with involvement on one side has some deficit on the other, but that might be hard to see because there isn't a normal side to compare with and because we know from autopsy evidence that PD always affects both sides.

In the original H-Y system there were no stages 1.5 and 2.5. These were added later as refinements. In stage 1.5, only one side is affected, but one can see symmetric problems on both sides such as reduced facial expression on both sides, stooped posture on both sides, or reduced arm swing on both sides. In stage 2.5 both sides are involved plus there is a mild impairment of balance, but not loss of balance. To test for this, the patient is told that he will be pulled backward and to take a step back to try to prevent a fall. The patient is then pulled backward firmly. It is considered normal to take one or two steps, but if three or more are taken and balance is recovered, it is considered stage 2.5 (or 1.5 if there are no signs of PD on the better side).

**Stage 3** refers to PD with impaired balance, defined by loss of balance when pulled backward so that the examiner must catch the patient to prevent a fall.

**Stage 4** is defined differently in different places. In some places it is defined by the need for an assistive device or a person to help walk, whereas in others it refers to severe impairment but where some walking is possible.

**Stage 5** means unable to walk.

The first problem with the H-Y staging is that it is based purely on mobility and takes no account of mental, behavioral or other non-motor problems. Since every study on health-related quality of life demonstrates that the most important determinants of quality of life in PD patients are non-motor, behavioral problems such as dementia, depression, fatigue, and sleep disorders, it may be irrelevant if the motor symptoms are mild but the patient is depressed and demented. His disease has severely altered his life, yet he may have stage 1.0, or seemingly mild disease.



The second problem has to do with the impact of the motor symptoms. A person may have stage 1.0, the lowest possible stage, with a small amount of tremor, a little slowness and reduced arm swing, but look and work normally; or the PD may be very severe on the one side so that one arm is almost useless but the other side is normal. If the affected side is non-dominant, for example the left side is affected in a right-handed person, the disease is annoying but may not interfere with work. The same stage, 1.0, affecting the right side may be completely debilitating. Yet, they are both stage 1.0

Unlike staging for cancer, higher stages may be less severe than lower stages. For example, a person who has minimal motor dysfunction but has it on both sides has stage 2.0, which might be far less severe than someone who has severe motor problems on only the dominant side. Similarly, someone with stage 3, meaning there is a balance problem, may have very mild motor dysfunction and have less impairment than someone with stage 1.0.

One can easily imagine many scenarios where a lower stage is associated with more severe disease than a higher stage. And even if we look at scoring systems like the Unified Parkinson's Disease Rating Scale, in which there is a point score each for tremor, rigidity, speech, slowness, etc, one sees the same confounding problems. For example, we rate tremor in each limb and the chin, from 0, meaning not present, to 4, meaning severe, and similarly for speech. Imagine someone who scores a 5 because there

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## G. FREDERICK WOOTEN JR., MD NAMED SCIENTIFIC & MEDICAL AFFAIRS ADVISOR

G. Frederick Wooten Jr., MD, former chairman of the Department of Neurology at the University of Virginia (UVA), Charlottesville, and internationally recognized authority on Parkinson's disease, has been named APDA's Scientific & Medical Affairs Advisor. He will head the association's program that has raised more than \$33 million for scientific research, and serve as the medical advisor for all of APDA's educational materials and programs.

"We are very fortunate that Dr. Wooten has agreed to serve in this position," said APDA president Joel A. Miele Sr., PE. "He not only is an internationally respected expert in Parkinson's disease but also has played a major role in APDA's growth and successes throughout the years."

Dr. Wooten, who has served as chairman of APDA's

Scientific Advisory Board since 1997, was one of the first recipients of its George C. Cotzias, MD, Fellowship, awarded to assist promising young neurologists in establishing careers in Parkinson's-related research, teaching and clinical services. He subsequently joined the UVA faculty, was appointed the Mary Anderson Harrison Professor of Neurology in 1982, and was named chairman in 1989. He also serves as the medical director of APDA's Information & Referral Center in Charlottesville.

The Alabama native is a renowned lecturer and visiting professor, author of more than 130 publications, and has written more than 30 book chapters, review articles and other publications.

## STAGING NOT IMPORTANT IN EVALUATING PD

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is a very minimal tremor in each arm, leg and chin. Compare this to a person with no tremor but speech which is totally incomprehensible, which would rate a 4. Thus, without seeing the actual patient, one would be misled to think that the person with a 5 was worse than the one with a 4, where the opposite is the case.

Severity of PD is currently not really measurable. We rate different aspects of PD differently and often use multiple different scales. It affects people in so many different ways that it defies methods for comparison, just as it has been impossible so far to measure what we mean when we say disease progression. We have good methods for measuring the motor symptoms of PD. We add points for tremor, stiffness, slowness, posture, walking, etc. and come up with a number, and that is how we currently test new treatments for PD.

Does the treatment reduce that number? Does it

slow worsening of that number? We also have methods for rating the non-motor symptoms, like pain, fatigue, sleepiness, and methods for rating the impact of the motor symptoms, such as drooling, penmanship, speech, but there is no single score than can capture the real impact of the disease. How should one compare someone whose speech is unintelligible but able to do almost anything else, to someone who can communicate clearly but has severe tremors and needs a walker?

The H-Y scale is useful for looking at populations of PD patients but is not useful for assessing a single person. It helps us understand how various treatments alter the progression of motor problems in large groups. The severity of your own PD is really a matter of how severely it affects your life. A number can never capture this.

*Dr. Friedman is a clinical professor, Department of Clinical Neurosciences, Brown University School of Medicine, Providence, R.I., and medical director of APDA's Rhode Island Information & Referral Center in Warwick.*



## EDUCATIONAL MATERIAL AND PATIENT SUPPORT RESOURCES

APDA is the source of a variety of many free educational and patient/caregiver support materials. Most publications listed below can be downloaded from the Web site, [www.apdaparkinson.org](http://www.apdaparkinson.org), publications page. Single copies are available by writing to the national office or calling 800-223-2732, faxing to 718-981-4399, or contacting any of the APDA Information & Referral Centers throughout the United States.

Free subscription to a monthly e-newsletter and "Tip of the Month" feature are available on APDA's Web site home page. Lotsa Helping Hands, a private, caregiving coordination service that allows family, friends, neighbors and colleagues to create an online community to assist a caregiver with daily tasks can be reached by clicking the "Ease the Burden" button.

APDA's National Resource Center for Rehabilitation provides direct telephone (888-606-1688) and email ([rehab@bu.edu](mailto:rehab@bu.edu)) access to a licensed physical therapist at Boston University's College of Health and Rehabilitation Sciences: Sargent College, to answer questions about exercise, provide information about programs in the caller's area and provide educational materials.



### BOOKLETS

(order by letter)

- |  |  |
|--|--|
| <b>A.</b> Parkinson's Disease Handbook             | <b>8.</b> The Family Unit and Parkinson's  |
| <b>B.</b> Young Parkinson's Handbook               | <b>9.</b> Maintaining Independence   |
| <b>C.</b> Be Active                                | <b>10.</b> The Challenge of Parkinson's Disease: Adapting to a Nursing Home                      |
| <b>D.</b> Be Independent*                          | <b>13.</b> Medical Management of Parkinson's Disease and Medications Approved for Use in the USA |
| <b>E.</b> Speaking Effectively                     | <b>16.</b> When Should Parkinson's Disease Patients Go to the Emergency Room?                    |
| <b>F.</b> Good Nutrition                           | <b>17.</b> Neuro-ophthalmology and PD  |
| <b>G.</b> Aquatic Exercise for Parkinson's Disease | <b>20.</b> Fatigue in Parkinson's  |
| <b>H.</b> My Mommy Has PD...But It's Okay!         | <b>21.</b> Dr. Andrew Weil's Recommendations for Healthy Aging                                   |

### SUPPLEMENTS

(order by number)

- |   |   |
|---|---|
| <b>4.</b> Keys to Caregiving  | <b>22.</b> Depression and Parkinson's   |
| <b>5.</b> Hospitalization of a Parkinson's Patient                      | <b>23.</b> Incontinence and Parkinson's |
| <b>6.</b> The Living Will and Durable Power of Attorney for Health Care | <b>24.</b> Employment and Parkinson's   |
| <b>7.</b> Parkinson's Disease and Oral Health                           | <b>25.</b> Constipation and Parkinson's |

\*Available by downloading from [www.apdaparkinson.org](http://www.apdaparkinson.org)

### FLYERS

- Basic Information about Parkinson's Disease
- National Young Onset Center
- Medications to Be Avoided or Used with Caution in PD
- 34 Helpful Hints to Improve the Quality of Life of People with Parkinson's
- The Importance of Having a Will

### WEB SITES

- [www.apdaparkinson.org](http://www.apdaparkinson.org)
- [www.youngparkinsons.org](http://www.youngparkinsons.org)

### DVD

- Managing Parkinson's: Straight Talk and Honest Hope, Second Edition