Depression and Anxiety
By Annette Schrag MD, PhD

Symptoms of depression and anxiety are common in Parkinson’s disease (PD), and depression scores are closely associated with patient-perceived health-status in PD. Approximately 30–40 percent of patients have significant depressive symptoms with lower prevalence rates in population-based studies. Anxiety affects up to 40 percent of patients.

Symptoms of both depression and anxiety can be off-period-related phenomena, which are usually, but not always, seen in parallel to motor fluctuations, and can then be particularly severe but respond to antiparkinsonian medication.

Both depression and anxiety can predate motor symptoms by several years and belong to the non-motor features that may herald the development of PD. While depression may occur reactively, or coincidentally, there is no doubt that at least in part it is an integral part of PD. The pathophysiology of these complications is complex and probably includes dopaminergic, serotonergic and noradrenergic mechanisms.

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APDA 2006 Cotzias Fellow Leads PD Cause Research Breakthrough

APDA 2006 Cotzias Fellowship recipient Clemens Scherzer, MD, has led a recent study showing that the brain cells in PD patients abandon the mitochondria, the body’s energy making machine. According to Dr. Scherzer, who is assistant professor of neurology at Harvard Medical School working with an international team of researchers, that shutdown can have devastating effects on brain cells.

The research, published in the journal “Science Translational Medicine,” shows that “a root cause of PD may lie in 10 gene sets related to energy production that spur neurons in the brain to “divorce” their mitochondria and related energy-producing pathways,” and indicates that boosting the mitochondria with FDA-approved drugs early on may prevent or delay PD onset.

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Dear Reader:

As another year begins to wind down and we begin to think about -- and start -- our holiday preparations, there is always the inclination to review what we have (or have not) accomplished -- a prelude to the subsequent resolutions.

At APDA we are looking back with gratitude and forward in hope.

Despite harsh financial restraints, we have continued to support our centers for advanced research, to meet our multi-year research commitments, and to provide funds to encourage young clinicians to look to research as a career. Our network of Information & Referral centers across the country remains intact, providing support and educational materials and programs, and developing new -- and maintaining existing support groups. We have even added two new free services for patients via our Web site: Lotsa Helping Hands, an online tool for caregivers; and the country's only Parkinson's rehabilitation resource center, providing physical therapy and exercise information via a hotline to Boston University's College of Health and Rehabilitation Sciences: Sargent College.

As anyone in charge of an operation knows, be it a business, a club or a home, one must take long hard looks at expenses, reducing dollars spent on non-essentials that do not affect the quality of our service. We continually seek new revenue streams, though that is more difficult as traditional sources are diminishing and even disappearing.

It is not easy to sit in a budget meeting and have to decide which program, which service, which research will be funded, and which we will have to postpone.

Only because of the continuous and generous contributions of our friends, those who believe in our mission, and the support of foundations -- not only to our national operations, but also regionally to local programs -- are we able to continue at mission.

This year, APDA-funded research revealed valuable information about the geographic and ethnic incidents of PD, and provided data for successful application for major National Institutes of Health funding. Our Young Onset program has grown in the quality of its programs and numbers being served.

In a few short weeks we will turn the page on 2010 and based upon hard work, planning and generous support will continue to serve Americans with Parkinson's disease and their families even better.

Joel A. Miele Sr., PE
President

Author Gail Sheehy Addresses Arizona Caregiver Conference

Gail Sheehy, author of "Passages," named one of the most influential books of our time" by the Library of Congress, was the keynote speaker at the Arizona Caregiver Consortium’s 15th annual Family Caregiver Conference in Tucson. Ms. Sheehy spoke about her new book, "Passages in Caregiving Turning Chaos into Confidence," based upon her 17 years of partnering in the care of her husband, New York Magazine founder Clay Felzer, who after several struggles with cancer, died in 2008.

The Nov. 12 conference in the Doubletree Hotel included a full day of outstanding speakers on numerous caregiver-related subjects.

November is National Family Caregivers Month
**Q:** My mother has PD and often feels as if she is “jumping out of her skin.” Also, her toes and feet cramp up. Are these symptoms of PD and what can be done to relieve them?

**A:** In answering this question, it would be very helpful to know if your mother is taking any medicine for PD and which ones she is taking. Also, do the symptoms you are describing occur in any relationship to the dosing of her medicines?

In general, yes these complaints can be related to PD itself or may represent motor and non-motor fluctuations related to dopaminergic medicines. We now recognize the non-motor features of PD which can include the kind of symptoms you are describing, i.e. “jumping out of her skin” may be anxiety or may be related to fluctuating levels of dopaminergic medications, termed akathisia (inner restlessness). The cramping of her feet and toes (dystonia) can represent either an “off” phenomenon or may represent a peak dose dyskinesia.

Keeping a diary in which she documents the time of medication administration and occurrence of these problems will help her neurologist to make medication adjustments in an effort to alleviate these complaints.

**Q:** I was recently diagnosed with PD and was prescribed Azilect. Are there any diet restrictions that I should be aware of?

**A:** Based on recent tyramine challenge studies with the approved doses of 0.5 and 1 mg per day there are no dietary restrictions. The original concern was that Azilect might inhibit both monoamine oxidase A and B (MAO). MAO-A does interact with tyramine and could cause significant cardiovascular problems. These recent studies support Azilect as a selective MAO-B inhibitor at the recommended doses and the FDA has removed any dietary warnings.

**Q:** My dad had deep brain stimulation and his cognitive abilities appear to be affected. Is this common?

**A:** The question of cognitive impairment after surgery depends in part on the patient’s pre-surgical mental status. If there is cognitive impairment before surgery then the likelihood is greater of having post-operative impairment. Formal neuropsychological testing is often performed prior to DBS surgery so that objective baseline evaluation can be undertaken. The data in general suggests possible mild memory impairment after surgery which is usually not clinically significant. Also, post-operative neuroimaging should be done to assure that no other lesions have taken place (stroke, hemorrhage etc.). Repeat neuropsychological testing may be helpful.

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**FDA Approves Generic Mirapex**

The Food and Drug Administration (FDA) has approved a generic version of Mirapex pramipexol dihydrochloride tablets, produced by Mylan, Inc.

The FDA move gives Mylan approval for 0.125-miligram, 0.25-miligram, 0.5-miligram, 1-miligram, and 1.5-miligram doses. The company already had approval from 0.75-miligram doses.

*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.*
IDENTIFICATION FOR TRAVELING PWP

APDA Executive Director Joel Gerstel was appointed to the Transportation Security Administration’s Disability Coalition in 2004 and has been working with representatives from more than 35 groups to provide insight into the needs of those with disabilities as they are screened at airports and other transportation checkpoints. His efforts included the publication of an incident of a person with Parkinson’s who was detained at an airport because he could not communicate and was assumed to be drunk. The traveler was not allowed to continue his trip, forced to take a cold shower, and to return to his place of origin.

Reports such as these have resulted in a newly issued TSA-approved card for use by people who have a disability, medical condition or medical device that may affect their security screening. The card, below, can be presented discreetly to the screener and, while it will not exempt anyone from screening, will make the officer aware of why movements and other behaviors are being caused.

The card can be clipped from this newsletter or downloaded from APDA’s Web site, www.apdaparkinson.org. It is not available at airports.

Depression and Anxiety

There is considerable evidence that dopaminergic dysfunction also plays a role. In addition, there is evidence from imaging studies that limbic noradrenergic/dopaminergic pathways are dysfunctional in PD patients with depression compared to those without. There also appears to be a genetic predisposition, as first-degree relatives of patients with PD are more likely to have had depression or anxiety.

Clinical Characteristics

The key characteristics of depression are low mood and lack of interest or pleasure, one of which is required for a diagnosis of depression in most classifications. Other features of depression can be present in varying combinations, but many of these, such as altered appetite or sleep, weight change, loss of libido, psychomotor retardations, reduced memory and loss of energy can overlap with the symptoms of PD, making diagnosis of depression in PD difficult.

Particularly in patients with advanced PD, there can be considerable difficulty in distinguishing somatic symptoms of depression from those of PD, such as slowness of movement and thinking, loss of appetite and weight, or sleep problems. The association with other symptoms of depression or PD and specific symptom characteristics (e.g. fatigability of movement in bradykiniesis vs. overall slowness in psychomotor retardation, the pattern of slowness in thinking in depression as opposed to that in cognitive impairment, or the temporal pattern of sleep disturbances and their association with immobility) can be helpful in distinguishing whether symptoms are due to PD or depression. However, this differentiation can be difficult even for an experienced clinician.

The most common anxiety disorders in PD are panic attacks (often during off-periods), generalized anxiety disorder (GAD), and simple and social phobias. Outside “off-periods”, that is no clear relationship to severity of motor symptoms or dementia, but anxiety may be part of an underlying depressive disorder. The relationship of antiparkinson medication to anxiety in PD needs further clarification. End Part 1. (Part 2: Management and Other Options in next issue.)

Dr. Schrag is a member of the faculty of University College’s Department of Clinical Neurosciences, London.
SLEEP DISORDER MAY PREDICT LATER PARKINSON'S DISEASE

Sleep disturbance is an established Parkinson’s disease (PD) problem reported by more than 75 percent of patients. Recent research at the Mayo Clinic in Rochester, Minn., and published in the Aug. 10 issue of Neurology, indicates that sleep disorders can precede neurodegenerative disease by decades.

While falling and staying asleep, vivid dreams, muscle stiffness, sleepwalking and headaches upon waking are typical PD-related symptoms, the published research found that vivid, violent dreams decades before a diagnosis can predict future neurological diseases.

The study led by Bradley Boeve, MD, concluded that REM (Rapid Eye Movement) sleep behavior disorder (RBD) may be one of the first PD predictors appearing years before other traditional physical symptoms such as tremor, slowness, or stiffness manifest themselves. Because of a lack of brain waves during REM sleep, muscle activity doesn’t occur in most people. Physical responses during the REM or dream period of sleep such as flailing, punching and kicking occur when part of the brain is damaged.

Dr. Boeve’s team examined the medical histories of 27 patients with a neurodegenerative disorder who had been diagnosed with RBD at least 15 years earlier.

END-OF-YEAR GIVING PROVES A WIN-WIN

While Congress argues the pros and cons of tax cuts, the fundamental truth is that end-of-year charitable gifts will mean reduced taxable dollars paid for 2010 personal income taxes. This applies to both regular income tax and those subject to the alternative minimum tax.

Giving can take several forms including a charitable gift annuity that can mean guaranteed life income for you while assuring your legacy in helping APDA’s mission. Rates are calculated by age, so the older you are, the more you will receive. (See box.)

The most common method of giving takes the form of cash, which can be used to eliminate up to half of the adjusted gross income (AGI) on an itemized federal return. Cash gifts can be made either by check or on APDA’s secure Web site, www.apdaparkinson.org. Some people prefer electronic transfers.

Securities that have been owned for more than one year and are worth more than their purchase costs are usually deductible to their full current value. Stocks, bonds and mutual fund shares are all eligible for up to a 30 percent tax deduction of an individual’s AGI. Securities that are currently less than their purchased costs can be sold, the proceeds contributed to charity with tax benefits on the loss as well as the charitable donation.

Planned giving through a living trust or including APDA in a will can serve as tax savings both short and long-term.

Age Does Have Its Rewards!

Rates for APDA gift annuities are calculated by age. The older you are, the more you get. You’re not only doing something good for yourself, but also you’re helping APDA Ease the Burden – Find the Cure.

Rates as of August 2010. Rates are subject to change at any time. Rates are also available for the two-life gift annuity. Call Executive Director Joel Gersté at 800-223-2732, ext. 120 to discuss annuities and other planned giving opportunities.

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JOHN HOPKINS RESEARCHERS FIND PROMISING PD DRUGS

Researchers at Johns Hopkins have shown that using specific drugs can protect nerve cells in mice from the effects of Parkinson’s disease (PD). The researchers’ findings are published in the Aug. 22 issue of Nature Medicine.

The newly discovered drugs block a protein that, when altered in people, leads to PD.

PD causes nervous system deterioration that leads to tremors and problems with muscle movement and coordination. There is no proven protective treatment yet. Only recently have genetic causes of PD been identified that have the potential to be used for developing targeted therapies for patients with the disease.

The protein LRRK2 (pronounced “lark 2”) is overactive in some PD patients and causes nerve cells to shrivel up and die. Why exactly overactive LRRK2 is toxic and leads to PD is still unknown.

Since overactive LRRK2 is deadly to nerve cells, researchers speculated that blocking LRRK2 from acting might protect them. The research team tested drugs that were commercially available and known to prevent proteins like LRRK2 from acting and adding chemical phosphates to other proteins. Out of 70 drugs tested, eight were found to block LRRK2 from working. Two of these eight previously were shown by others as able to cross the blood-brain barrier. So the researchers injected these two drugs twice daily into mice engineered to carry Parkinson-causing LRRK2 changes in the brain.

After three weeks, the researchers examined the mouse brains to see if nerve cells had died. One drug provided almost complete protection against nerve cell death. Another drug had about 80 percent fewer dead cells than in mock treated mice. A third drug, which does not inhibit LRRK2, was not effective.

“The data suggest that if you were to develop a safe drug, then you could potentially have a new treatment for Parkinson’s disease patients with LRRK2 mutations,” said Ted Dawson, MD, PhD, professor of neurology and physiology and scientific director of the Johns Hopkins Institute for Cell Engineering.

The two drugs that blocked LRRK2 and prevented death of nerve cells in mice with PD both had similar chemical structures. “One could envision generating compounds around that core structure to develop a relatively selective and potent inhibitor of LRRK2,” said Dawson, who is collaborating with researchers at Southern Methodist University to design more specific inhibitors of LRRK2, and the group plans to license this technology.

Once they identify promising candidate drugs, those candidates will have to be tested for toxic side effects. The drugs’ approval by the FDA for use in humans may still be many years away.

Dawson added, “Treatments developed specifically against LRRK2 may even be able to treat other forms of Parkinson’s disease — those not caused by LRRK2 alterations — as there may be several alterations in different proteins that can lead to PD.

“We’re curing Parkinson’s disease in a mouse and now we have to discover drugs that actually work in human neurons. Then we’ll hopefully be able to make the leap forward to get a treatment to work in humans.”

Teva Pharmaceuticals Seeking Clinical Trial Participants

Teva Pharmaceuticals is seeking participants for a clinical research study to determine if an investigational add-on drug helps to control Parkinson’s Disease (PD) symptoms. Eligible participants must have a confirmed PD diagnosis, currently be taking a form of Requip® or Mirapex®, be 30 years of age or older and feel that their current treatment is not doing enough to control their symptoms.

Individuals who qualify for the study and wish to participate may receive study medications and study-related medical exams at no cost, compensation for time and travel and study-related care from a local clinical research physician.

For more information call 1-800-887-8100 or visit www.researchforpd.com.
PUT THE FREEZE ON FREEZING

APDA’s Parkinson’s Rehabilitation Resource Center, located at Boston University’s College of Health & Rehabilitation Sciences: Sargent College, has received more than 500 calls on its free Helpline (888-606-1688) since its inception less than a year ago.

According to the center’s director, Terry Ellis, PD, PHD, NCS, many of these calls asked about walking and freezing. “About one third of people with Parkinson’s disease experience freezing episodes, sudden short, transient blocks of movement that occur primarily with initiating walking, turning, navigating through narrow spaces or approaching obstacles,” she explained. “Freezing can last just a few seconds or up to several minutes. Freezing can limit household and community mobility, increase risk of falling and contributes to reduced socialization and quality of life.”

Dr. Ellis and her staff have produced a one-page resource, “Ten Tips to Put the Freeze on Freezing!” Its suggestions are:

1. Try another movement – raise an arm, touch your head, point to the ceiling; then restart.
2. Change direction: if you can’t move forward, try stepping sideways and then go forward.
3. Carry a laser pointer in your pocket; when you freeze, shine the laser in front of your foot and step on the light. This cue can help you restart.
4. Visualize an object on the ground in front of you and try to step over it.
5. Wear a metronome on your belt or carry a small one in your pocket. Turn it on and the external beat can help you restart.
6. Try humming a song and time your restart with the beat of the music.
7. Count “1-2-3-go” and then step forward.
8. Shift weight side to side to help initiate taking a step.
9. March in place a few times and then step forward.
10. Don’t fight the freeze by trying harder to step forward. Shift your attention from moving the legs to moving the arms, then resume walking forward.

The center can also be reached by e-mail, rehab@bu.edu, or by direct link from APDA’s home page, www.apdaparkinson.org. The 10 freezing tips can also be downloaded from the site.

Sleep Disorder May Predict Later Parkinson’s Disease

The median interval between RBD and the diagnosed neurological disorder was 25 years, with one case preceding a PD diagnosis by half a century.

Only one in nine patients was female, reflecting the predominance of men with PD. Previous studies had revealed that RBD was not an isolated disorder, and that anywhere between 80 to 100 percent of these patients developed a neurodegenerative disorder later in life. According to Dr. Boeve, however, no one knew just how long and finding such long intervals between diagnoses was unexpected.

In a Science News story, he noted, “In the neurodegenerative realm, we just don’t know any other clinical manifestations that can start so far in advance.”

Identifying early warning signs, the study’s authors hope, will allow treatment before motor and non-motor degeneration begins.

In the meantime, Roseanne DeFranzo Dobkin, PhD, assistant professor of psychiatry at UMDNJ, Robert Wood Johnson Medical School, New Brunswick, N.J., recommends that PD patients currently having sleep difficulties discuss the symptoms with their doctors and seek appropriate treatment. She notes that an overnight evaluation in a sleep clinic may identify specific causes of insomnia. Only then can the appropriate treatments be ordered.

Intermittent sleep medication may be prescribed, and daily exercise, relaxing before bedtime and keeping regular sleep hours may also help, as will avoiding excessive time in bed, daytime naps, caffeine or alcohol in the evening, and large evening meals.
Educational Material and Patient Support Resources

AFDA is the source of a variety of free educational and patient/caregiver support materials. Most publications listed below can be downloaded from the Web site, 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@bv.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)

A. Parkinson’s Disease Handbook
B. Young Parkinson’s Handbook
C. Be Active
D. Be Independent*
E. Speaking Effectively
F. Good Nutrition
G. Aquatic Exercise for Parkinson’s Disease
H. My Mommy Has PD...But It’s Okay!

SUPPLEMENTS
(order by number)

4. Keys to Caregiving
5. Hospitalization of a Parkinson’s Patient
6. The Living Will and Durable Power of Attorney for Health Care
7. Parkinson’s Disease and Oral Health
8. The Family Unit and Parkinson’s
10. The Challenge of Parkinson’s Disease: Adapting to a Nursing Home
13. Medical Management of Parkinson’s Disease and Medications Approved for Use in the USA
16. When Should Parkinson’s Disease Patients Go to the Emergency Room?
17. Neuro-ophthalmology and PD
20. Fatigue in Parkinson’s
21. Dr. Andrew Weil’s Recommendations for Healthy Aging
22. Depression and Parkinson’s
23. Incontinence and Parkinson’s
24. Employment and Parkinson’s
25. Constipation and Parkinson’s

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
• www.youngparkinsons.org

DVD

• Managing Parkinson’s: Straight Talk and Honest Hope, Second Edition

*Available by downloading from www.apdaparkinson.org

The printing and distribution of this newsletter are supported by a grant from Novartis