



The American Parkinson Disease Association

SPRING 2007 NEWSLETTER

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PARKINSON'S DISEASE IN WOMEN

By Susan M. Rubin, MD

Clinical Instructor and Director of the Women's Neurology Center at Glenbrook Hospital, Glenview, Illinois

Until recently little has been written regarding the effect that gender has on the development and management of Parkinson's disease (PD). Current research has focused mainly on the impact that sex hormones have on the development of the disease. Less has been written on the impact that Parkinson's disease has on menstruation, pregnancy and menopause. This article will review the most recent information on both the affect that Parkinson's disease has on women and the impact that gender has on Parkinson's disease.

While PD is usually thought of as a disease of the elderly, approximately 3-5 percent of women diagnosed with this disorder are under the age of 50. A large number of these women are still experiencing regular menstrual cycles. Studies that have reviewed the effect of hormone fluctuations and menstruation on PD have noted an impact of the menstrual cycle on disease control. During menstruation women described increasing Parkinson symptoms, decreasing medication responsiveness, and increased "off" time. They also complain of increased fatigue, cramps and heavier menstrual flow. This can lead to occasional humiliating self-care issues because of worsening dexterity. Premenstrual symptoms of depression, bloating, weight gain and breast tenderness also appear to increase in intensity in women who note a variation in their symptom control with menstruation.

Usually these symptoms improve after menstruation, but will reoccur with each cycle. A small sample of women in the studies used birth control pills. They reported that they had less intense fluctuations in their symptom control, but more research needs to be done before recommendations

can be made. However, it is important to recognize that these fluctuations occur so that women can be prepared for the changes in control. The use of regular exercise and relaxation techniques can help decrease symptoms and improve coping abilities.

There have been only a limited number of pregnancies in women with PD reported. The data have been divided into the impact that pregnancy has on Parkinson's disease and the effect that Parkinson's disease has on pregnancy. There is an increase in both motor and non-motor symptoms during pregnancy although it is rarely significant enough to impact the women's overall level of functioning. Non-motor symptoms (such as fatigue, constipation and depression) seem to improve after delivery, but any progression of motor symptoms (rigidity, slowness of movement and tremor) usually persists. While data has shown that increasing length of estrogen exposure (the amount of time from puberty to menopause) decreases the risk of developing PD, increasing amount of time spent pregnant seems to increase the risk of developing PD. This seems contradictory but may be due to differences in the effect that estriol (the pregnancy form of estrogen) and estradiol (the menstrual form of estrogen) have on the disease.

The main concern of pregnant women with PD is the risk of birth defects from antiparkinson's medications. The dopamine agonists, bromocriptine and pergolide, are considered relatively safe during pregnancy, but make it impossible to breast feed because they block milk production. The remainder of the antiparkinson's medications carries a category C rating, meaning that animal studies suggest some risk but human studies are not available or
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VINCENT N. GATTULLO
PRESIDENT

Dear Reader,

With calendar years and different fiscal, religious and cultural years, it is sometimes a challenge just to know what time zone you are occupying. At APDA we of course, begin the calendar year with a resounding "Happy New Year," while our fiscal year begins Sept. 1 and ends Aug. 31. With a nod to the Chinese Year of the Pig (which began Feb. 18), and in recognition of the Jewish Rosh Hashanah and Christian Advent in September and December respectively, I somehow think of our Parkinson's year as beginning in April, and as we go to press with this issue, we are in the middle of celebrating in style.

Each April our awareness and research fund-raising efforts grow - a tribute to the thousands of chapter presidents and members, I&R center coordinators, support groups and volunteers who make up our national network. Through walk-a-thons; awareness days; local exhibits and regional symposia; state, city and township proclamations; and collaborative support of our advocacy and fellow PD organizations, APDA is in the forefront of efforts to eradicate the disease and support those already diagnosed.

It is also the time - I think appro-

priately - that our Scientific Advisory Board convenes to discuss and recommend research funding for the coming year - fiscal year, that is. These 15 eminent physicians and scientists volunteer their time and knowledge to assure that the funds raised by our grassroots partners are used to their most promising potential.

So, April, the month of Dr. James Parkinson's birthday and the official Parkinson's Disease Awareness Month, is a special, high-energy time for us at APDA, and in the coming months we will report the successes of your efforts and the research that has been selected to be supported.

On a sad note, I share with you the passing of John Haugen, APDA treasurer for the past seven years. John was a quiet, compassionate and charitable man whose loss will be felt not only by APDA but also by the many other organizations he served and people whose lives he touched. Our sympathies go to his wife, Sophia, and his family.

Vincent N. Gattullo
President

SUBSPECIALTY NEUROLOGIC EXTERNSHIP

By Tom Viviano,
Coordinator APDA I&R Center
Banner Good Samaritan Medical
Center, Phoenix, AZ

Banner Good Samaritan Medical Center in Phoenix, AZ is pleased to announce an opportunity for physicians to enhance their knowledge of Parkinson's disease. (PD) The new Subspecialty Neurologic Externship in Parkinson's disease will be supported by a grant from the Arizona Chapter of the American Parkinson Disease Association.

The course will allow hands-on experience with patients, as well as provide time for attendees to ask questions of the neurologists and therapists who comprise the course faculty.

Trained in Movement Disorders, faculty neurologist Padma Mahant, MD and Johan Samanta, MD see Parkinson's patients in their private practice, and at the Good Samaritan Neuroservices Clinic. They are also the Medical co-Directors of the APDA Information & Referral Center in Phoenix.

According to Dr. Mahant, "This an outstanding opportunity for physicians to fine tune their skills, while experiencing the most up to date therapies and research. We appreciate the support of the APDA and the efforts of their program coordinator, Tom Viviano, in helping to attain CME certification for the externship, as well as in developing promotional materials for this new teaching tool."

The course is free of charge to U.S. licensed neurologists, and offers 5.5 category 1 CME credits to attendees. Interested professionals can contact Tom Viviano at the Phoenix APDA I&R Center by calling 602-239-3542 for more information. ■

A PATIENT'S EXPERIENCE WITH CLINICAL TRIALS

BY JEAN BURNS, Person with PD, PD Advocate for the Parkinson's Action Network and Volunteer for Arizona-APDA



I was diagnosed with Parkinson's disease (PD) in January 2003. I immediately tried to find out everything I could about the disease. I learned that it is progressive and incurable, but I kept telling myself there must be something I could do to fight it. It was then that I stumbled across "clinical trials" as I searched the internet.

I found a listing of clinical trials for PD and located the ongoing studies in my area. I focused on one in particular with the potential to be neuroprotective because it had shown promising results in primates. It had also shown to be safe in the initial trial on humans.

The key criterion to join the trial was to not have begun any PD medications. While my doctor had urged me to start on PD medicines, I had refused to take any because my symptoms were not yet debilitating.

I printed out the trial information and made an appointment with my neurologist. When I showed him the info he read it with interest. He's never heard of the trial, but said that I met the profile. He asked that if I did sign up for the trial, to let him know.

I found it interesting and alarming that he hadn't known anything about the clinical trial. Why hadn't he? Here was a trial with great promise - to slow or stop the progression of PD! If I got the drug, and it worked, I'd have the opportunity to get it years before the general population - years during which the progression of this horrible disease would be slowed down, or even stopped.

So why hadn't my doctor informed me about clinical trials? I thought it should have been an option for my treatment. Why had I been the one to inform him?

In 2005, the Advancing Parkinson's Trials campaign conducted a Harris Poll to determine why so few people with Parkinson's (PWP) participate in clinical trials and identify what barriers there were keeping PWP from participating. There were some surprising results from the poll:

Nearly all (95 percent) of the patients who were surveyed agreed that clinical trials for Parkinson's are necessary to find better treatments, yet only 11 percent reported their doctor ever suggested participating in a trial.

Of those PWP surveyed who were aware of trials, only 11 percent had received information about trials from their doctors.

About 40 percent of the PWP surveyed had learned about trials from support groups, and 27 percent had learned about trials from other PWP.

Only 14 percent of primary care physicians, 21 percent of neurologists, and 18 percent of PWP surveyed indicated that they were some-

what or very satisfied with the amount of information available about clinical trials for Parkinson's disease. Only one percent of PWPs participated in clinical trials.

The current number of PWP who participate in clinical trials and studies is far short of the number that researchers anticipate will be needed over the next two to three years for new trials. Because of a growing concern within the Parkinson's community about low levels of participation in trials, PDtrials was created.

PDtrials is an educational effort initiated by a consortium of national Parkinson's organizations, led by the Parkinson's Disease Foundation. Its purpose is to increase information and awareness about clinical trials. The Web site, www.Pdtrials.org, is an excellent source for people with Parkinson's to find current information about clinical trials.

Volunteer for PDtrials. You may see me at a local event handing out pamphlets from PDtrials, and answering questions.

There are many types of clinical trials for PD:

- Neurorestoration:** These trials focus on ways to restore the brain cells damaged by Parkinson's disease.
- Neuroprotection:** These trials focus on slowing down or stopping the progression of brain cell loss.
- Movement symptoms:** These trials focus on tremors, rigidity, freezing attacks, difficulty walking, loss of fine motor control, and balance problems.

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BY ENRICO FAZZINI, DO, PhD
 Assoc. Prof. Neurology
 New York University, New York, NY,
 University of Nevada, Las Vegas, NV,
 N.Y. Institute of Technology, Old Westbury, NY.

Q: Six years ago I was diagnosed with Parkinson's disease. Currently I am taking Requip 4 mg, Sinemet 25/100 and Comtan 200 mg four times a day. At night before bed I take one Sinemet 50/200 and one Comtan 200 mg. Recently I have experienced shortness of breath and difficulty breathing during "off" episodes. I am unable to move at this time. What should I do?

A: During your "off" episodes your muscles become rigid. This includes the muscles of your chest wall. You may experience restricted breathing when this occurs. You need to do one of the following: take your doses closer together, increase the Requip, add another medication such as selegiline or rasagiline, and/or pay strict attention to the timing of your meals and doses. Consult your doctor for the best option considering your specific medical history.

Q: I am an 82 year old retired physician who has been diagnosed with Parkinson's disease now for the past five years. Up until last July my symptoms were relatively mild, but suddenly in late July the symptoms became severe and progressive. My neurologist tried several different combinations and dosages of medications, but none seems to be very helpful. I received your winter newsletter this past week and read it thoroughly and found it most interesting. My neurologist has me on Stalevo 100 mgm six times a day: 7 am, 9:30 a.m., noon, 2:30 p.m., 5

p.m., and 7:30 p.m. If I am awake during the midnight period, he has me take Sinemet 25/100. One of your articles says that some cases require as often as three hour dosages. I am taking a Stalevo every 2¹/₂ hours. So, does my dosage seem too close together? I have mild nausea, which I attribute to the dopamine in the medication. My most troublesome symptom is twitching of my left leg - this may last for a long period. My question is this: since my last dose of Stalevo is 7:30 p.m. and my first dose is 7 a.m., there is a gap in medications of almost 12 hours. Surely this causes a low level of medication during the night. It seems that the dosage should be spread out more evenly for the 24 hour period. I would appreciate your comment on this.

A: Neurotransmitters and hormones peak in the morning upon awakening and slowly decrease during the day. Sleep has a rejuvenative effect on your brain. Medications are dosed in such a way as to mimic what occurs naturally. Medications help you to move and you should have this benefit during the day when you are active. Excess medication may lead to insomnia, excessive dreaming and even hallucinations and we, therefore, want to avoid dosing late at night. In other words, it is common to take Parkinson's disease medications during the day and to avoid taking them from the evening until the next morning.

Q: My brother has Parkinson's. So far the only noticeable sign to me is his slowness of movement. He is under doctor's care. My question is: Is it possible for PD to cause extreme leg pain? My brother has this when he walks or stands for any length of time. He was in the past told it was not related to PD, however, the pain is increasing, and there are no answers as to what it could be. He just finished extensive testing with all kinds of specialists at Lahey Clinic in Massachusetts. In the end, they simply said they have no idea what is wrong with him. The only thing he is aware of is that one of his protein counts is extremely low. He is now going to have that tested.

A: Leg cramps are extremely common in patients with Parkinson's disease and often occur on the same side where the Parkinson's disease symptoms started. Young patients (onset less than 50 years old) are especially vulnerable. The cramps consist of the big toe turning up, the little toes turning down and the entire foot turning inward. The cramps may occur during times when medications wear off, but can also occur when the medications are working too much. Attempts must be made to stabilize the medications (start or increase dopamine agonists, take less immediate-release Sinemet, add Comtan, rasagiline/selegiline, controlled-release Sinemet and add anticholinergics and/or benzodiazepines. Botox/Myobloc injections may also help. ■

F.Y.I. is a guide to the efforts and successes and recognition of the hundreds of volunteers and staff who work daily to help ease the burden and find a cure for millions of persons with Parkinson's and their caregivers across the United States.

The VA's Commitment to Veterans with Parkinson's Disease

BY REBECCA MARTINE, APRN, CS, BC
Chairperson, National VA PD Consortium
Associate Director of Education,
Philadelphia PADRECC



In 2001, the Department of Veterans Affairs (VA) set upon its mission to revolutionize services for the approximated 40 thousand veterans afflicted by Parkinson's disease (PD). The first tier of this campaign focused on the establishment of the Parkinson's Disease Research, Education and Clinical Centers (PADRECCs). Six Centers of Excellence were founded at the Philadelphia, Richmond, Houston, West Los Angeles, San Francisco, and Portland/Seattle VA Medical Centers. Each PADRECC is designed to deliver state-of-the-art clinical care, pioneering research, and educational programs to an expansive geographic region. Internationally recognized movement disorder specialists and researchers staff these Centers. In 2003, the PADRECCs introduced the National VA Parkinson's Disease Consortium in an effort to promote PD awareness across the universal VA Healthcare System. This initiative has focused on professional networking, men-

torship, and training. The Consortium is currently composed of more than 225 members, including physicians, nurses, pharmacists, social workers, physical and occupational therapists, and other allied health professionals. Membership is free and encouraged for all VA providers. The Consortium Center Network was subsequently launched in 2006 as a means to broaden the impact of the PADRECC mission. These 41 designated Centers grant veterans convenient access to specialized movement disorder services by spanning the length of the country. The PADRECCs and Consortium Centers now create a hub and spoke model of care that is highly innovative and effective. All veterans enrolled in the VA Healthcare System are eligible for services at a PADRECC or Consortium Center. Additional information on these programs, including directions on how to obtain an appointment, can be found at www.parkinsons.va.gov or by calling 1-800-949-1001 x2749. ■

PADRECC Coordinating Centers:

215-823-5800 x2238

415-221-2485

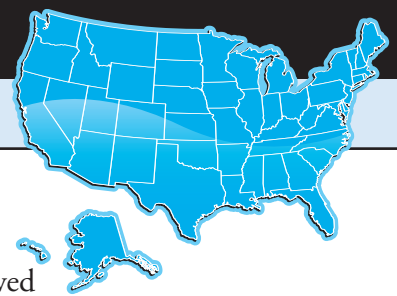
Consortium Coordinating Center:

215-823-5800 x2238

Ed. note: APDA makes its educational materials available free of charge at all PADRECC centers.

Pergolide Withdrawn From US Drug Market

Pergolide (Permax® and generic) is being voluntarily withdrawn in the United States because of concerns that heart valve disease may result from long-term use of the drug. This announcement was made by the United States Food and Drug Administration (FDA) on March 29, 2007. This withdrawal will be gradual, allowing patients and physicians to switch patients to another treatment. ■



IN THE WEST

When ground was broken for the Lou Ruvo Brain Institute in Las Vegas recently, APDA executive director Joel Gerstel was among the invited dignitaries including the governor and former governor of Nevada, congressmen, councilmen and **Las Vegas** Mayor Oscar Goodman.

Gerstel was among the invited dignitaries including the governor and former governor of Nevada, congressmen, councilmen and **Las Vegas** Mayor Oscar Goodman.



APDA executive director, Joel Gerstel, had a moment to chat with world-renowned architect Frank Gehry at the Las Vegas groundbreaking.

men, councilmen and **Las Vegas** Mayor Oscar Goodman.

The world-renowned architect Frank Gehry designed the \$50 million facility focusing on research and treatment of

Alzheimer's, Huntington's and Parkinson's diseases, ALS and memory disorders, and will be the new home of APDA's Las Vegas Information & Referral Center when completed in 2009. Dr. Zaven Khachaturian, a leading Alzheimer's authority, will head the Institute, which includes a medical advisory board that includes Nobel Laureate, Dr. Paul Greengard, of the Rockefeller Institute, and Dr. Ronald Peterson of the Mayo Clinic, who cared for former president, Ronald Reagan during his last years.

Gehry, whose iconic designs have been described as, "not being able to be ignored - applauded or derided - but not ignored," worked 11 months before presenting his rendering of the 60,000 square foot multi-functional building last year.

The concept of a center for scientific research began a dozen years ago at a dinner to honor Las Vegas businessman and philanthropist Larry Ruvo's dad, Lou Ruvo, who died of Alzheimer's, and has evolved into one of the city's largest fundraisers.

IN THE NORTH

Science Daily (SD) recently reported on the work of Subhojit Roy, MD, PhD, a neuropathologist and research associate at the **University of Pennsylvania**, and APDA 2006 post-doctoral grant recipient. Dr. Roy's novel video-

imaging system has allowed researchers at the university to observe the transport of the protein alpha-Synuclein moving along axons, important in the understanding of PD. According to SD, "Understanding this process of axonal transport is important for studying many neurodegenerative diseases." In 1990, APDA funded research led to the discovery of alpha-Synuclein at the Robert Wood Johnson Medical Center, New Brunswick, N. J.

Teams from 10 schools across **Long Island**, N.Y. participated in Mattituck (N.J.) High School's varsity wrestling team's "Takedown Parkinson's Wrestling Tournament" recently. Coach John Roslak has been sponsoring the event for several years and – with his mom, who had PD and is the annual walk-a-thon's top fundraiser, – has raised thousands of dollars for PD research.

IN THE EAST

Linda O'Connor, Cedars-Sinai Medical Center (**Los Angeles**) I&R coordinator was featured in an interview about serving PD patients in nail salons. Linda's hands-on advice appeared in "Nailpro" magazine's February article, "What You Should Know About Parkinson's Disease to Best Serve Your Clients".

The biggest question for those attending the **Seattle** Chapter's fifth annual Magic of Hope auction/dinner was which of the many items to bid on. On the auctioneers block at the St. Demetrios Orthodox Greek Church was everything from a seven-day cruise to a night patrolling Seattle with the Police K-9 Division, with a country club golfing day, a three-day resort getaway, and a private wine/hors d'oeuvres tasting for 45 of your closest friends.

IN THE MIDWEST

A University of Wisconsin, Madison, theatre class and Lee Silvers Voice Therapy therapist Sherri Sleazy have worked together to produce 'Parkinson's Playhouse,' a two-act play addressing the communications problems faced by PD patients. Coordinator Jessica Hahn is seeking funding to have the two-hour, "no-holds-barred" production, which includes an audience-participation discussion, videotaped and converted to a DVD. After its successful first night at the university, there is discussion of taking it on the road throughout the state. ■

APDA OPENS NATIONAL CENTER FOR YOUNG ONSET

Because of the growth and identified needs of the young onset Parkinson's disease (PD) patients, the American Parkinson Disease Association (APDA) has created a national young onset center at Glenbrook Hospital, Glenview, Illinois, to increase national awareness of the many services available to the younger PD population. Julie Sacks, MSW, LCSW, is the director.

APDA opened the country's first Young Onset Information & Referral (I&R) Center in 1991 in Santa Maria, Calif. Arlette Johnson, a Parkinson's patient, served as its coordinator

until her retirement four years later. During that time, she initiated programs and services specifically for younger PD patients and their families including the first dedicated PD young onset Web site. In 1994, the center was relocated at Glenbrook Hospital and named the Arlette Johnson APDA Young Onset I&R Center with Michael Rezak, MD, PhD, its medical director and Susan Reese, RN, LCSW, its part-time coordinator.

Dr. Rezak, who is the director of the Movement Disorders Center and Functional Neurosurgery Program at Evanston Northwestern

Healthcare, will serve as the new center's medical director.

Ms. Sacks has extensive clinical and administrative experience as a social worker and has successfully developed programs and support for their growth. She also brings experience in advertising and marketing and will use both with current technology to increase awareness of PD and its effects on younger people. She has supervised master's level social workers and has the professional experience to understand and support the psychosocial challenges young people with PD may face. ■



A MESSAGE FROM THE APDA NATIONAL YOUNG ONSET CENTER DIRECTOR

It is my pleasure to join APDA as the director of the new Young Onset Center.

I have a somewhat unusual combination of education, training and experience, all of which have prepared me for exactly this role. I am a Licensed Clinical Social Worker with more than 10 years experience working with individuals of all ages and their families. Before receiving my Master of Social Work degree, I earned a Bachelor of Arts degree in communications and worked in advertising and marketing for eight years.

My professional experience will be helpful in identifying and understanding the particular concerns young people with PD face and also in developing new programs and services that will address those needs. It is my objective that every person who receives a young onset PD diagnosis will at the same time be told about our Center and leave the physician's office knowing he or she is not alone.

Please keep in mind that anyone, anywhere is encouraged to contact us. If we are not the appropriate place, we will connect you with the APDA Information & Referral Center in your region. In fact, that is one of our center's primary functions - to connect people with local resources.

I'm looking forward to your call.
Julie Sacks, MSW, LCSW
877-223-3801

Flower Power for Parkinson's

40% donation to PD research

Help APDA in the fight against Parkinson's disease. Make a visible statement and a 40% donation to Parkinson's research at the same time.

We have chosen the breathtaking red tulips with a small white edge, the traditional symbol of hope for Parkinson's disease. These mid-spring bloomers produce egg-shaped flowers on 20-to-24-inch stems and are appropriate for planting in containers for balconies and patios as well. Packages contain 25 top-size bulbs, and make wonderful gifts.

The best part is that APDA will receive 40 percent of the price (excluding shipping costs) of every package of tulips purchased. So, when planting your beautiful tulip bulbs, you are also planting hope for the cure.

Share this offer with friends and family and help Parkinson's research even more. The price per bag, \$29.95, includes all shipping and handling charges. Orders must be received by September 15, 2007.

How easy to order:

1. Order online at www.tulipworld.com/APDA
2. Call toll free 1-800-688-9547

APDA
TO END THE SILENCE, TALK ABOUT IT.
WWW.APDA.ORG

LONG TERM CARE IS A CONCERN OF PD PATIENTS

While there are many technical definitions, long-term care is basically the help needed to get through the day for an extended period of time – months and even years. It can include skilled medical care but more often involves help with daily activities such as walking, toileting, bathing, eating and dressing.

Long-term care can be given at home, in the community, in congregate settings, and in nursing homes, and more than 40 percent of people receiving such care in this country are under age 65. Americans spend more than \$123 billion each year in formal long-term care, a number that is increasing by \$2.6 billion every year.

Today, publicly available options for funding long-term care for Parkinson's disease patients are severely limited. Very few private health insurance plans cover it and Medicare does not cover most nursing-home stays and pays less than 2 percent of long-term care expenses. Medicaid is part of the welfare system, and is only available after spending down your assets to state-required levels.

For information about long-term care insurance available for patients with Parkinson's disease diagnosis contact apda@apda-parkinson.org. ■

TWO NEW CENTERS BRING I&R NETWORK TO 62

APDA's Information & Referral Center network grew to 62 centers recently with the opening of newcenters at the University of Kentucky (UK) School of Medicine, Lexington, and the University of Texas Health Center, Tyler. John Slevin, MD, director of the UK school's movement disorder clinic, is the medical director, and Renee Wagner, RN, is the coordinator. The Texas center is being directed by George Plotkin, MD, PhD, with Kelly Pierson, a clinical trial research specialist, coordinator.

In St. Louis, Deborah Guyer, a certified speech pathologist and former APDA St. Louis chapter member, has replaced Jan Meyers as I&R Center coordinator at Washington University. ■



IS FOR AWARENESS IN THE APDA ALPHABET

If there are people unaware of the challenges and heartaches that Parkinson's disease brings to a family, it is not the fault of APDA chapters, I&R centers, support groups and volunteers.

Parkinson's Disease Awareness Month was filled with APDA activities from coast to coast, from Maine's fifth annual Parkinson's Awareness Conference in South Portland to a 5K walk and fun run in San Diego.

Connecticut's Lunch & Lecture Series featured "The Ten Commandments of Coping with Parkinson's Disease," and "Parkinson Disease Management & Research Update" with lunch in between.

Seven governors proclaimed April Parkinson's Awareness Month in their states: Mike Beebe (Ark.); Edward Rendell (Pa.); Jodi Rell (Conn.); Charlie Crist (Fla.); George Perdue (Ga.); Deval Patrick (Mass.) and Tim Pawlenty (Minn.). Chicago (Ill.) Mayor Richard Daley, Tulsa (Okla.) Mayor Kathy Taylo, and Little Rock (Ark.) Mayor Jim Dayley issued city proclamations. In addition dozens of townships, boroughs, and congressional proclamations across the country were issued and reported in local media. ■



What a difference a year makes. Georgia coordinator Mary Louise Weeks believes strongly in taking her child to work, making Charlotte Louise Weeks probably the youngest person to have had two visits with a governor before her first birthday.



THE DIRECTION OF PARKINSON'S DISEASE RESEARCH

BY JACOB SAGE, MD,
DIRECTOR, APDA CENTER FOR
ADVANCED PARKINSON'S RESEARCH
UMDNJ-RWJMS
NEW BRUNSWICK, NJ

The last decade in Parkinson's disease (PD) research has seen a major shift in emphasis from the study of ways to ameliorate symptoms toward ways in which to protect neurons from early death. In order to protect neurons we must first understand what are the causes of cell death in Parkinson's disease.

There are two major candidates for this causative role, genetic factors and perhaps environmental factors.

Genetic factors are so far more firmly established as causes contributing to the onset of Parkinson's disease. To date there are mutations in five genes that are known to be associated with PD. These genes are alpha synuclein, Parkins, PINK 1, DJ-1, and LRRK-2.

Mutations in these genes, however, account for only a small number of patients and we must find other factors that play a role in the majority of patients.

It is likely that the most important gene found so far is the alpha synuclein gene. When one looks under the microscope at the brains of patients with Parkinson's disease, the hallmark of the pathology is a cell

marker called the Lewy body. These Lewy bodies contain large amounts of the protein called alpha-synuclein even in patients who do not have a mutation in the alpha synuclein gene. It looks as if aggregates or clumps of alpha-synuclein (termed protofibrils) may be toxic and responsible for cell death in Parkinson's disease. Parkinson's disease can therefore be considered a synucleinopathy, that is a disease of abnormal accumulation of alpha synuclein in the brain. This accumulation appears to be the central defect that causes Parkinson's disease in most patients. Looking at ways to decrease alpha synuclein protofibrils in PD patients may be the key to neuroprotection and to slowing the progression of the disease.

A number of different mechanisms may be playing a role in cell degeneration by affecting alpha-synuclein.

1. There is a mechanism of cell degeneration that has been described as "programmed cell death," also called apoptosis. Aggregates of alpha-synuclein directly and indirectly increase cell death by apoptosis. By using drugs that interrupt the pathway that leads

to this type of cell death, we might be able to achieve neuroprotection.

2. The parts of cells called mitochondria (which produce the energy to drive the cell) have decreased activity in the brains of patients with Parkinson's disease. The specific part of the mitochondria that is affected is called complex I. Decreased activity of mitochondria leads to increased aggregates of alpha synuclein and thereby increases cell death rates by apoptosis. Drugs that can increase complex I activity may slow the progression of Parkinson's disease by keeping the energy metabolism at a normal rate. They are the basis for directing new treatments.

3. Biochemical reactions called oxidation reactions have been shown to increase the rate of cell death by causing increased aggregation of alpha synuclein in the parts of the brain involved in Parkinson's disease. Drugs that reverse or slow these oxidation reactions may therefore slow the progression of the disease. Such drugs (called antioxidants) are available but so far none has been proven effective in slowing the progression of disease.

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APDA Is America's Largest Grass Roots PD Organization

APDA is the country's largest grass roots organization serving the Parkinson's community. It is a 501(c)(3) not-for-profit organization and receives no governmental or public funding. Each year APDA contributes more than \$2.5 million for research and more than \$2.5 million for direct patient and caregiver support through the generous support of individual and corporate donations. You can be a partner in easing the burden and finding a cure with a tax-deductible gift to the American Parkinson Disease Association, Inc. Call 1-800-223-2732 for details. ■

THE DIRECTION OF PARKINSON DISEASE RESEARCH *(cont. from pg 9)*

4. There are increased deposits of iron in the brains of patients with Parkinson's disease. Heavy metals are known to increase the aggregation of alpha-synuclein. Finding ways to decrease brain iron deposition, therefore, may slow the cell death rate.

5. Dopamine itself may increase aggregation of alpha-synuclein and, therefore, finding more effective ways to increase dopamine levels in the brain may be helpful in slowing disease progression. Researchers are beginning to focus on the fact that PD is not just a disease of the dopamine system of neurons but is a widespread disease involving many neuronal groups and systems in the brain. Clinicians have been acutely aware of this fact from the beginning. Patients with PD not only have motor difficulties but also may have significant problems with depression, concentration, and other cognitive functions such as decision making processes, constipation, autonomic functioning in areas as wide apart as blood pressure control and sexual function, skin changes, sleep and more. The emphasis, therefore, is now shifting to finding causes of cell death in general and not just looking at cell death in dopamine producing neurons. Some of the other gene mutations listed above may play a part

in a more widespread role of keeping cells alive or causing them to die. There is some evidence for example that the DJ-1 gene may be crucial in keeping cells from entering the death pathway (apoptosis) and mutations in the gene may somehow facilitate entry into the cell death pathway and in this way may contribute to the onset of PD. How might this knowledge of gene mutations be put to use in treating PD? Recall that genes produce proteins and abnormal genes produce abnormal proteins which may influence events in many cell in the brain. Even if we are unable to fix the gene defect itself, we might be able to use drugs or other strategies to counter-effect the abnormal protein. For example, if the effect of an abnormal protein were to decrease energy efficiency in brain cells, we could possibly devise ways to get around the defect and increase energy metabolism and thereby keep those cells alive. In fact, one possible use of stem cells might be to provide agents that bathe brain cells with the necessary growth factors to keep them alive. This strategy would have a more generalized beneficial effect than would the strategy of merely providing cell replacement for cells already lost. Based on some of the arguments presented here, there are several neuroprotection studies currently in progress and more being planned. These studies enroll patients in the early stages of disease but if successful they will undoubtedly help all patients with PD. ■

Adapted from the Summer 2006 Newsletter of the APDA New Brunswick, NJ I&R Center Newsletter.

A PATIENT'S EXPERIENCE *(cont. from pg 3)*

•**Non-movement symptoms:** These fatigue, depression, difficulty in speaking, and loss of facial expression, vision changes, and a diminished sense of smell.

•**Genetic:** These trials investigate possible hereditary connections to the disease and often take place over long periods of time.

There are always new clinical trials starting. If you check www.Pdtrials.org and don't find one today that is a match for you, check back in a couple of months. There may be something new by then. Don't give up! Remember that no new treatment (and no cure) will be available until it has completed clinical trials. Please consider joining one.

My own clinical trial story unfortunately ended in disappointment. After having participated for two years, the trial was abruptly halted because it had failed. The people who got the drug actually deteriorated slightly faster than the people on the placebo! (I learned that, I had received the lowest dose of the drug rather than the placebo.)

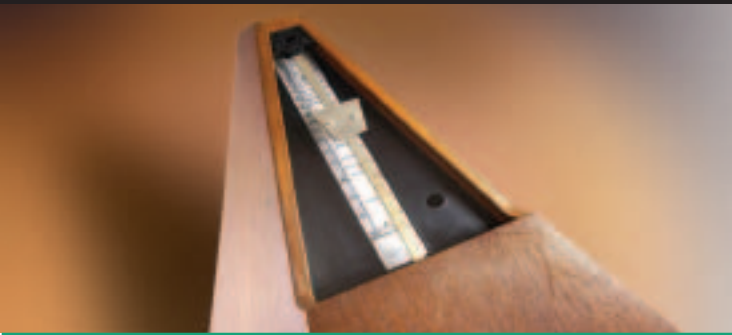
These results illustrate there is no guarantee about positive results when you join a clinical trial. Even though I had done extensive research prior to joining the trial, learning the drug had shown great promise-it failed.

Regardless of the trial's failure, I am philosophical about my participation. If the drug had worked as hoped, I'd have been jubilant, as would have been my comrades in the trial. As it turned out, I was glad I had been taking the lowest dose. In the end, the experience won't keep me from joining future trials. I'll do the same extensive research and take my chances.

I hope to see you soon to talk to you about PDtrials. ■

Adapted from the APDA Arizona Chapter Winter Newsletter, January 2007





METRONOME THERAPY- AN EFFECTIVE TREATMENT TOOL FOR PARKINSON'S PATIENTS

BY KRISTINE BROWN,
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Interactive Metronome Therapy (IM) is a new technology used as a treatment tool for Parkinson's patients, but it is actually based on an old concept - the metronome. For any of you who have ever played piano, you know that the metronome is a device used to keep time-tick-tock, tick-tock... if you think about it, doing the same task over and over again at a perfectly consistent interval requires a lot of concentration and energy. With Interactive Metronome therapy, a Parkinson's patient is trained to do just that - to keep time by performing repetitive tasks such as clapping their hands or stomping their foot at regular intervals. The IM signals the patients with a cowbell-like ring to let them know if they are either falling behind or going too fast in their task. While these tasks might appear simplistic, the Interactive Metronome measures accuracy down to the mil-

lisecond and it is surprising how challenging it really is to achieve a perfect score!

The goal of Interactive Metronome therapy is to improve symptoms of Parkinson's patients struggling with issues such as rate of processing, attention, impulsivity, speech, and cognition. There appears to be a positive correlation between the increased accuracy of patients in their IM therapy sessions and their improved Parkinson's symptoms.

Michael Lobell, MD, a Tucson physician and Parkinson's patient currently undergoing IM therapy, attests to its efficacy with diminishing his Parkinson's symptoms. He said, "The reason that I came to HealthSouth initially was for impulsivity. Since I began my speech therapy, my entire outlook has changed. My impulsivity is better and my speech patterns are slower. The Interactive Metronome seems to be an effective and important

tool."

While IM therapy is relatively new, it is gaining popularity worldwide. There are more than 2,000 IM-certified therapists in more than 1,500 clinics, hospitals and universities in the U.S. and abroad. It has also received media attention by the CBS Early Show, CNN News, and US News and World Report. The Interactive Metronome therapy is an option for patients who are seeking new ways to complement their existing treatment regimen without adding new medications.

A typical course of treatment with IM is 10-12 sessions and each session will last approximately one hour.

For further information on where the therapy is available, call 877-994-6776, ext. 230.

Adapted from the January 2007 Winter Newsletter of the APDA Arizona Chapter ■

(cont. from pg.1)

have not confirmed that risk. The data on levodopa with or without carbidopa suggest some risk in animal studies, but there were no reported birth defects in newborns in the small number of pregnancies reviewed. Amantadine is the only antiparkinson's medication that has resulted in heart malformations in babies with first trimester exposure. There were no reports of major malformations with the use of Selegiline (Eldepryl) and there are data available so far on the COMT inhibitors.

Women with PD do not have trouble with fertility but can have changes in self-image that lead to social avoidance and difficulty with sexual intimacy. This can lead to decreased pregnancy rates and sexual dysfunction. Women

who do become pregnant must then face the challenge of caring for a child postpartum. The American Parkinson Disease Association offers resources and helpful staff to provide information and support regarding pregnancy and parenting issues related to PD. Establishing a support system and planning are critical to being an effective parent, especially if you have a progressive disease.

It has been noted that women are more likely to develop Parkinson's disease later than men and usually when they are postmenopausal. Basic science research with rats has shown that there is an increase in the slow decline in dopamine producing cells coincident with menopause. Use of hormone replacement in rats that have had their ovaries

(cont. on pg.12)

Information on Parkinson's Disease

Single copies of the following publications may be obtained free of charge by writing to the national APDA office or by calling the toll-free number 1-800-223-2732 or faxing to 1-718-981-4399, or contacting any of the 62 APDA Information and Referral Centers.

EDUCATIONAL BOOKLETS

1. **Basic Information about Parkinson's Disease**
Brochure (English, Chinese, Spanish, Portuguese, Russian)
2. **Parkinson's Disease Handbook**
Symptoms, causes, treatment; 40-page booklet (English, German, Italian)
3. **Be Active** - A suggested exercise program for people with Parkinson's disease; 25-page booklet (English)
4. **Be Independent**- Equipment and suggestions for daily living activities; 22-page booklet (English)
5. **Speaking Effectively** - Speech and swallowing problems in Parkinson's disease; 34-page booklet (English)
6. **Good Nutrition** - 20-page booklet (English)
7. **Young Parkinson's Handbook** - 78-page booklet (English)
8. **How to Start a Parkinson's Disease Support Group** - 24-page booklet (English, Italian)
9. **Aquatic Exercise for Parkinson's Disease** - 20-page booklet (English)
10. **Next Step After your Diagnosis** - 23-page booklet (English)
Finding information and support
11. **My Mommy Has PD... But It's Okay!** - 20-page booklet for young children.

EDUCATIONAL SUPPLEMENTS

Caring for the Caregiver: Body, Mind and Spirit; The Family Unit; The Fine Art of "Recreation & Socialization" with PD; Medical Management of PD; Vision Problems and PD; Treatment of PD; Fatigue in PD; Healthy Aging.

DVD

Managing Parkinson's - Straight Talk and Honest Hope.
Created by the Washington State Chapter of APDA especially for newly diagnosed Parkinson's patients and their loved ones. Leading experts explain what PD is and how it is treated, how to deal with symptoms of the disease, some of the medications' side-effects and how to keep a positive outlook in dealing with it.

APDA WORLDWIDE WEB SITE

www.apdaparkinson.org for PD I&R Centers, Chapters, Support Groups, education and information material, meeting dates, publications, medical abstracts, clinical trials and research application guidelines.

WORLD PARKINSON DISEASE ASSOCIATION WEB SITE

www.wpda.org. A weekly updated source of world news.

(cont. from pg.11)

removed seems to reverse that increase. However, studies in women have had contradictory results showing only partial or no benefit from hormone replacement. This may be the timing of the hormone replacement, since the animal studies have shown a difference in benefit based on the timing of the hormone supplement. Rats who received hormone supplements within 10 days of having their ovaries removed had no increase in the loss of dopamine producing cells, while rats that did not receive estrogen until 30 days later did lose cells more rapidly. They did not see any benefit from the supplements in the rats who received them later.

The few studies that have compared the impact of hormone replacement therapy on disease progression have been mildly positive. Women on hormone replacement reported more "on" time and lower UPDRS scores than non-estrogen users. Unfortunately the number of women studied is too low to support the use of hormone replacement in women with Parkinson's disease at this time. The benefits still need to be weighed against the risks recently reported in the Women's Health Initiative study.

In conclusion, we are beginning to understand the impact of sex hormones on the development and progression of Parkinson's disease. Recent studies suggest that there is an inverse relationship between lifetime estrogen exposure and the risk of developing Parkinson's disease. It has also been shown that fluctuations in hormone levels will result in changes in disease control and result in the need for changes in symptom management during menstruation, pregnancy and menopause. Hopefully, we will gain further understanding in the future which will lead to new treatment options for women with Parkinson's disease. ■

Adapted from the Winter 2005 issue of the APDA Young Onset Information & Referral Center Newsletter in Glenview, Illinois.

Materials concerning the research in the field of Parkinson's disease, and answers to readers' questions are solely for the information of the reader and should not be used for treatment purposes, but rather as a source for discussion with the patient's health provider.