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**VA Research News**

**a. PD Research Appropriations**

On April 23, 2004, Michael J. Kussman, M.D., Acting Deputy Under Secretary for Health, Department of Veterans Affairs, testified in a hearing held by the House Veterans' Affairs Subcommittee on Oversight and Investigations about current research being conducted by VA on Alzheimer's, Parkinson's, and Diabetes. He reported, "Over the past five years, VA funding for Parkinson's disease research has nearly doubled, with \$10.1 million allocated for projects in FY 2004. Since FY 1999, non-VA funding has more than doubled, with VA investigators leveraging over \$6.4 million in non-VA funds in FY 2003. The funded projects focus on various aspects of Parkinson's disease research, including:

- the role of neurotransmitters other than dopamine,
- advances in neuroimaging technologies to monitor disease progression,
- stem cell and fetal transplantation research in animal models,
- gene therapy in animal models,
- mechanisms of damage to nerve cells,
- non-motor aspects of Parkinson's disease,
- rehabilitative strategies for Parkinson's disease, and
- clinical trials of surgical treatment for refractive Parkinson's disease."

For more information on the hearing please go to the House Committee on VA website at [www.veterans.house.gov/hearings/schedule108/apr04/4-28-04/witness.html](http://www.veterans.house.gov/hearings/schedule108/apr04/4-28-04/witness.html)  
<<http://www.veterans.house.gov/hearings/schedule108/apr04/4-28-04/witness.html>>

**b. Total Research Appropriations**

In FY 2004, Congress approved an appropriation of \$408 million for VA research and development. More than \$650 million will be contributed to VA research from other government and non-government sources. Today, VA supports studies by more than 3,800 scientists at 115 VA facilities across the country. (Source: *Department of Veterans' Affairs VA Research Fact Sheet*, March 2004)

**Parkinson's Disease Gene Discovered in UK**

Researchers at London's Institute of Neurology have identified a Parkinson's gene after studying three families from Italy and Spain who had several members with early-onset PD. When they analyzed DNA from the families, they discovered mutations in the PINK 1 gene that provides coded instructions for a protein that affects chemical reactions within cells. This protein

dysfunction reduces the ability of brain cells to protect themselves from stress. Further research will be directed toward what the protein does normally, as well as when it is mutated, and what specific role the gene may play in PD. The lead author, Dr. N. Wood was quoted: "This discovery opens the door to a whole new area of PD, and perhaps other neurodegenerative disease research." (Source: *Science*, April 16, 2004).

### **DHEA Boosts Growth Rate of Stem Cells**

DHEA or dehydroepiandrosterone is among the most abundant naturally occurring steroids in the blood of young humans, but levels decline with age and its physiological effects on humans are poorly understood. Svendsen and Suzuki, scientists of the U of WI at Madison learned that human neural stem cells, exposed in a lab dish to DHEA, exhibited an uptick in growth rates suggesting that the hormone may play a role in helping the brain produce new cells. They noted a significant increase in the division of the cells. This increase in the number of neurons produced by the stem cells prompted an increase in the neurogenesis of cells when the DHEA culture was compared with a non-treated culture. Although the findings are new, there is a possibility that DHEA could play a role in moderating the genesis of new brain cells. (Source: *Proceedings of the National Academy of Sciences*, Feb. 18, 2004).

### **Parkinson's Risk Higher for Men**

The observation that PD affects more men than women has a long history dating back several hundred years. The most likely culprit for a gender gap may be a genetic mutation passed down by their mothers. These mutations have been located on the X-chromosome where men are more vulnerable to genetic changes than women. Men may be at greater risk also because of a Parkinson-linked mutation of a gene found in mitochondrial DNA, a tiny reservoir of DNA found outside the nucleus that is passed down via the mother to her children. Other theories suggest that the male lifestyle (pesticide exposure and head injury) may account for the difference and that estrogen may protect women against neurological diseases such as PD. (Source: *Journal of Neurology Neurosurgery and Psychiatry*, March 17, 2004).

### **Theories About Pesticides and PD**

Previous reports have suggested that exposure to various pesticides raises the risk of PD. Now, new research indicates that the risk is even higher in patients with a certain gene variant. In the body, many pesticides are broken down and made less toxic by an enzyme called cytochrome P450D6. A certain variant in this CYP2D6 gene has been shown to produce an enzyme that is less effective at breaking down pesticides. As a result, people with this variant may be more susceptible to pesticides that might cause PD. Out of 247 PD patients and 676 healthy subjects in this French study, the risk of PD was 2-4 times higher for those who had no normal copies of CYP2D6, only variants. (Source: *Annals of Neurology*, March 2004).

### **Reports from the AAN Meeting in San Francisco, CA, April 2004,**

#### **a. Chronic GDNF Offers Sustained Benefit in Advanced PD**

Studies of glial cell line-derived neurotrophic factor (GDNF) in rodent and primate models of PD have suggested that it exerts a broad range of neuroprotective and neurorestorative effects. Scientists in London injected the substance directly into the posterior dorsal putamen in 5 patients with advanced PD. Clinical improvement was sustained for at least 2 years for a chronic infusion of GDNF as measured by the UPDRS and F-dopa positron emission tomography at baseline and at 6-month intervals for 2 years. It is expected that future research will test the clinical implications of these findings.

#### **b. Apomorphine as Rescue Therapy in PD**

Recently, the FDA approved apomorphine (Apokyn) to be given by injection and to be administered with an anti-nausea drug. Many research trials over a period of 3-5 years preceded this approval. One of these trials presented at the AAN Conference involved Dr. Koller and colleagues from Mt. Sinai Medical Center. They treated in the dose-titration phase 56 advanced PD patients (multiple daily "off" periods) with escalating doses, 2-10mg, of apomorphine followed

by a crossover phase that began when the 4mg. level was reached (n=51). The UPDRS was the primary outcome measure. The median change from predose UPDRS was significant following 4 mg injections of apomorphine at 20, 40 and 90 minutes. The major adverse events were mild to moderate and included yawning, dizziness, nausea, and sedation. Recently, the FDA approved apomorphine (Apokyn) to be given by injection and to be administered with an anti-nausea drug.

### **c. The Effect of Cognitive Impairment and Psychosis on QOL in PD**

Shulman and colleagues from the U of MD School of Medicine evaluated the effects of motor fluctuations, dyskinesias, psychosis, and cognitive dysfunction on activities of daily living (ADLs), Instrumental ADLs (IADLs) and Quality of Life (QOL) in patients with PD. In a study of 224 patients, the presence of cognitive impairment or psychosis made more of a difference in daily function and QOL than either motor fluctuations or dyskinesias. The researchers concluded that interventions that focus on cognitive difficulties and psychosis may have more of a dramatic impact on the patient's ability to carry out ADLs and IADLs than would relief of motor complications.

(Source: *Fishman, P. Ed., Neura-on-site, Daily Report*)

### **Clozapine Curbs Psychosis in Parkinson's Patients**

Low-dose clozapine may be helpful in reducing psychotic symptoms brought on by drugs commonly used to treat patient with PD. Dr. Pierre Pollack and colleagues in France conducted a study of 60 patients with PD who were randomized to receive a daily dose of 12.5 to 50 mg of clozapine or placebo. This was followed by a 12-week open clozapine period, plus a one-month period after drug discontinuation. Outcome measures included the clinical global impression scale, the positive and negative symptom scale, the UPDRS, and the MMSE. Drowsiness was seen more often with clozapine treated patients, but the rate of other adverse events did not differ between the groups. The researchers concluded that clozapine at a dose of less than 50-mg. per day improves psychotic symptoms "without significant worsening of motor function." Source: *Journal of Neurology, Neurosurgery and Psychiatry* May 2004: 689-695.

### **Movement Disorder Society (MDS) Sponsors Workshop in Chicago.**

A major issue facing clinicians is the management of the complications of advanced PD. A regional course offering, jointly sponsored by the MDS and the NIA/Foundation for Advanced Education in the Sciences, Inc. (NIH/FAES), will be held in Chicago, IL on Aug. 28, 2004. This workshop will provide an overview of motor complications and treatment for advanced PD. This course is interactive and will include video case management for some sessions. For more information, contact [joliva@movementdisorders.org](mailto:joliva@movementdisorders.org) <<mailto:joliva@movementdisorders.org>>.

### **Free PD Educational Kit Available**

Novartis Pharmaceutical Corp. has announced the availability of a new, free-of-charge information and resource kit designed to help educate persons living with PD and their families. "Managing PD" was developed in consultation with the American Parkinson Disease Association (APDA) and the National Parkinson Foundation (NPF), the Parkinson's Disease Foundation (PDF) and the Parkinson Alliance (PA). To obtain a free kit, call toll-free 1-866-783-7548 or visit [www.stepkit.net](http://www.stepkit.net) <<http://www.stepkit.net>>.

### **New Exercise Video to Help PD Patients**

"Motivating Moves for People with Parkinson's" is a new seated exercise program sponsored by the Parkinson's Disease Foundation (PDF), and produced and directed by nationally recognized movement specialist, Janet Hamburg. The innovative program is available in video and DVD formats and targets the major symptoms of PD including stability, flexibility, posture, vocal projection, and facial expressivity. Cost is about \$15 and can be ordered through [www.pdf.org](http://www.pdf.org) <<http://www.pdf.org>>. (Source: *PDF News*, Winter 03-04)

### **Houston PADRECC News**

For Veterans and Family Members - On Thursday, June 3<sup>rd</sup>, at 6:00 PM, the PADRECC Patient and Family Forum will feature a program of inspiration and photography. Two individuals

with PD who have exhibited in the Houston FotoFest 04 will display a selection of their photographs. This will be followed by a presentation and a panel of patients and caregivers discussing: "Living with Parkinson's Disease: Patient and Family Connections." Contact Naomi Nelson at 713-794-8938 for more information.

For Allied Health Professionals - On Saturday, June 12<sup>th</sup>, our PADRECC Allied Health Symposium will address "Cognitive Issues and Depression in Patients with Movement Disorders: Implications for Treatment.". Continuing education credits will be offered for PT, OT, SLP, and Social Work. For further information, contact Marilyn Trail at 713-794-7287 or Naomi Nelson 713-794-8938.

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