This is the news;etter for May of 2007 minus masthead

An Extraordinary Day

Stan Wertheimer

On 3 March 2007 The CPWG sponsored a forum on clinical trials at the UConn Medical Center in Farmington, CT. Planning had been in the works for nearly a year, under the leadership of Tom Sullivan and Pat Sullivan. Clinical trials were chosen as the topic of this first major presentation of CPWG because of the crucial role they play in the search for a cure. As Marshall Loeb, member of the board of directors of the PDF and former managing editor of both Fortune and Money magazines, put it in the PDF newsletter:

> *Some great day in the future, medical science will declare that at long last a cure has been found for Parkinson's. We do not yet know what that cure will entail and require. But we can be reasonably certain that a significant part of it will be the result of widespread clinical trials — the sometimes daunting, always exciting testing of laboratory ideas on human subjects.*

Spectrum, the IND newsletter reported:
The Connecticut Parkinson's Working Group (CPWG) in collaboration with [*a better way to put it might be "with the blessings and support of" – ed*] the University of Connecticut Health Center, PDtrials.org and the Parkinson's Disease Foundation (PDF), hosted nearly 250 people affected by PD today at a forum held at UCONN Health Center.

The speaker panel included PD experts from four research centers in Connecticut. Dr. J. Antonelle de Marcaida of Eastern Connecticut Neurology Specialists and Dr. Adam Simmons of the UCONN Health Center Department of Neurology co-moderated. Dr. de Marcaida explained that the intent of the forum organizers was "…to demystify clinical trials and …to encourage everyone in the PD community to feel ownership in the academic work being done to defeat PD." The forum showcased the wealth of expertise in PD that is in Connecticut and the spirit of collegiality and cooperation between the various research centers.

In addition to IND's own Dr. Danna Jennings, the panelists included Dr. Mohammed N. Hassan from UCONN Health Center's Department of Neurology, Dr. Bahman Jabbari from Yale University's Department of Neurology, and Dr. John Murphy from Associated Neurologists in Danbury. Panelists, each covering a different focus on the process of bringing new medicines to the public, provided a clear understanding of the necessary role of clinical trials, and at the same time underscored some of the enormous challenges.

Dr. Jennings, in her analysis of some of these challenges, discussed some of the changes in the pharmaceutical industry over the past 25 years. In 1980 it cost $2 billion to make 34 new drugs available to patients. By 2000, the cost had risen to ultimately reverse PD and diseases like it. The energy and commitment of people with PD in Connecticut so well demonstrated at this event is a hopeful sign for the future of PD research in the state.

Pat and Tom Sullivan and the CPWG deserve to be commended for an excellent job in organizing and managing the event. The CPWG was founded in 2000 by Stan Wertheimer ["*cofounded by Stan Wertheimer and Jackie Dorwin*" – ed]. Its mission is to provide education and support to those affected by PD and to collaborate with the medical community to enhance treatment and research of Parkinson's disease. They're doing a terrific job.

It should be pointed out that the other speakers, not from IND, did an equally fine job of discussing their topics. All panelists fielded questions enthusiastically and with attention to the level of the audience. It was an extraordinary day.

Parkinson's is on the rise

As population ages, number of people with age-related ills up, with 80% increase of disease by 2030

BY JAMIE TALAN Newsday Staff Writer January 30, 2007

The numbers of people growing old and living longer have led to ominous projections for PD. By 2030, there may be 80 percent more Americans with the disease, and the numbers will double in developing Asian nations, according to a new study.

Dr. E. Ray Dorsey and his colleagues at the University of Rochester say the prevalence will grow as populations shift in age. In 2005, there were an estimated 4.1 million people worldwide with PD . In 25 years, that number is predicted to climb to 8.7 million.

"This is a chronic condition that will be claiming more and more people," said Dorsey, co-author of the study published this month in the journal Neurology. The scientists said the growth will be greater outside the U.S. China and India have growth curves that are more like a triangle, with more young people than older ones. Over time, this will tip the scales as the young population ages and leave more people vulnerable to PD and other age-related diseases like Alzheimer's.

"They are absolutely on target," said Dr. Warren Olanow, professor and chairman of neurology at Mount Sinai School of Medicine in Manhattan, referring to the new study. "This will certainly be a bigger public health issue. Not only will more people develop PD but patients will have it longer and remain disabled by it. "

He suspects there are close to a million people in the U.S. with PD. Olanow recently testified before Congress that the movement disorder costs society $27 billion a year in medical bills and lost wages. "This new study illustrates the personal, family and social problems this will represent," he added.

PD is primarily an age-related disease. Symptoms take hold when most of the dopamine-containing cells in a brain region called the substantia nigra die away. But while medicines that target the brain chemical dopamine offer relief in the early days of the disease, in time they stop working effectively. The treatments don't seem to help the gait disturbances, freezing, falling and dementia that follow the path of this disease.

The answer, Olanow and Dorsey agree, will come from more research and new treatments that protect against PD, or slow its course. PD researchers now know it isn't only dopamine-containing cells at play in the progressive illness. Olanow said PD is characterized by other pathologies spread throughout the brain. Work is now under way to develop drug treatments – including gene therapy and stem cell therapy – to stall the disease process.

Alzheimer's disease is far more common, with about 4.5 million patients in the U.S. By 2030, this number is expected to double. In the U.S., the proportion of the population over 65 was 12.4 percent in 2000 and expected to jump to 19.6 percent in 2030, according to the Centers for Disease Control and Prevention.

Parkinson Disease Study Announcement

A study is being conducted about communication between PWP and their partners. The study is for couples that have been living together in a marriage-like relationship for at least 5 years. There is no age limit for participants. Other study criteria are:

1. The PWP must be on some form of *levodopa* medication.
2. The PWP experiences moderate to advanced problems due to his or her PD.
3. All participants must be able to read and understand an 8th grade level of English.

around a long time, and a large number of people have potentially been exposed to them," said Dr. Michael S. Okun, medical director of the NPF. And the drugs are much more widely used in Europe and developing countries because they cost less than newer drugs that do the same thing, he added.

Some patients who have done well on pergolide will decide to continue to take it, Okun said. Valeant Pharmaceuticals International of Aliso Viejo, which markets pergolide under the brand name Permax, said in an e-mailed statement that "Permax is a safe and effective treatment for patients with PD . Although Valeant no longer promotes the product, we still make it available for those who prescribe it."

Similar heart valve problems led to the withdrawal of the diet drugs fenfluramine and dexfenfluramine — part of the now notorious fen-phen drug combo — from the market in 1997.

The drugs cause the heart valves to develop fibrous deposits that produce leakage of blood back into the heart. That causes the heart to overwork, which can lead to heart failure and death. The problem is readily detected by ultrasound and can be fixed only by replacing the valve.

Roth, who has a contract with the NIH to screen every drug on the U.S. market for the heart valve problem, said he had found other drugs that present the same problem. He would not identify them, however, pending the publication of his initial results.

PD , which strikes as many as 100,000 Americans each year, is characterized by severe tremors and rigidity in the limbs, and loss of muscle control. It results from the death of brain cells that produce the neurotransmitter dopamine (DA), which plays a key role in transmitting commands from the brain's muscle-control centers.

The most commonly used treatment is the drug levodopa, which is converted to DA in the brain. Pergolide and cabergoline are members of a family of drugs called DA agonists that bind to DA receptors in the brain and produce effects similar to DA.

The use of pergolide in this country was declining even before the heart valve risk became known because of the development of newer DA agonists, including pramipexole and ropinirole, said Dr. Fernando Pagan of Georgetown University. The new results make it more important for neurologists to steer patients away from pergolide and toward the newer agents, he said.

In one study, Dr. Renzo Zanettini and his colleagues at the Istituti Clinici di Perfezionamento in Milan, Italy, used echocardiography to study 155 patients taking the two drugs and found "clinically important" valve damage in 23.4% of those taking pergolide and 28.6% of those taking cabergoline. None of those taking other DA agonists showed the problems, they said. Their study was funded by two Italian Parkinson's foundations.

In the second study, Dr. Rene Schade of Charite-Universitatsmedizin in Berlin studied patients with newly diagnosed cardiac valve problems. They found that pergolide increased the risk sevenfold and cabergoline fivefold, while other DA agonists did not raise the risk.

Skin Patch Eases Parkinson's Symptoms (02/28/2007)

(01/03/07) WASHINGTON (Reuters) – In a recent study, a skin patch relieved symptoms of people with early stage PD, and may offer advantages over taking pills to treat the disease. The study, involving 277 people in Canada and the United States with early stage PD, assessed the ***Neupro*** patch, made by Germany's Schwarz Pharma. It delivers a drug called rotigotine, a dopamine(DA) agonist.

Patients who wore the patch showed a significant easing of their symptoms after six months of treatment, according to the report in the journal Neurology. Those getting a placebo saw their symptoms get worse. Schwarz Pharma funded the study: the patch is applied once a day and delivers rotigotine continuously through the skin. Currently, many patients take pills several times a day to treat symptoms.

"I think it's an important new development for PD patients. For a significant portion, this may

offer real advantages," Dr. Ray Watts, chairman of the University of Alabama at Birmingham's Department of Neurology and leader of the study, said.

PD affects nerve cells in the area of the brain that controls muscle movement, and is characterized by a shortage of the neurotransmitter DA. Rotigotine imitates the effects of DA and helps make up for the shortage.

"The study didn't directly compare the patch with pills currently used to treat PD. It was unique in testing a new delivery system for a DA-related drug," Watts said. "The patch can provide a steady dose over 24 hours, allowing for a more uniform delivery of medication to the brain than pills might provide," he added. He went on: "Patients who are doing well now, may or may not see an advantage to switching But for newly diagnosed patients, especially younger ones who are going to be treated for a long time, the patch may be more important."

Schwarz Pharma official Michael Davis said the company expects to win approval from the FDA for the patch to treat early stage Parkinson's disease in the first half of this year.

Diabetes Linked To Higher Parkinson's Risk 02 Apr 2007

People who have type 2 diabetes are more likely to develop PD as they age, though researchers are uncertain what accounts for the link between the two diseases, according to a new study being published in the April issue of ***Diabetes Care***.

The study, by researchers in Finland, is the first large prospective study to find type-2 diabetes to be a risk factor for PD. According to the authors, people with type 2 diabetes are 83 percent more likely to be diagnosed with PD than people in the general population. The study found the association between the two diseases existed for both men and women, independently of other confounding factors.

"Diabetes might increase the risk of PD partly through excess body weight," the researchers hypothesized, since their work showed that excess body weight was also associated with an elevated risk of Parkinson's disease. However, they concluded that more research needed to be done to fully understand the mechanisms behind this link.

Diabetes Care is published by the ***American Diabetes Association***,

Parkinson Disease and Cholesterol 2/8/2007

De Lau LM, Koudstaal PJ, Hofman A, Breteler MMB. Serum cholesterol levels and the risk of Parkinson's disease. Am J Epidemiol *2006;164:998-1002.*

A study has shown that women who have higher levels of total cholesterol in their blood have a lower chance of developing Parkinson disease.

Why is this study important?

In people who have Parkinson disease, nerve cells that make dopamine die off. Why these cells die is not known with certainty, but two important factors are believed to be "mitochondrial dysfunction" and "oxidative stress." Mitochondrial dysfunction means that cells have a problem with the way that they use nutrients to create energy. Oxidative stress is caused by exposure to various substances in the environment, such as chemicals or cigarette smoke, or by infection. These exposures result in cell damage.

A chemical called coenzyme Q10 helps to lessen the effects of mitochondrial dysfunction and oxidative stress. The body naturally produces coenzyme Q10, which is present in all cells, including nerve cells. Levels of this chemical decrease with age and have been found to be lower in some people with chronic diseases such as Parkinson disease. (Small not-well-designed studies on the use of coenzyme Q10 supplements have suggested that this substance may be helpful in decreasing the symptoms of Parkinson disease.) Researchers have also recently discovered that

blood levels of cholesterol and of coenzyme Q10 are related. Cholesterol is a fat that is present in the membranes of all cells and is also necessary for nerve cells to work properly.

Who were the researchers and what did they do?

Dr. de Lau and his coworkers in the Netherlands measured the levels of cholesterol and a genetic marker called *APOE* in the blood of 6,465 people aged 55 years and older who were taking part in the Rotterdam Study. All of the participants filled out a form about how much coffee they drank, whether they currently or had ever smoked, what medicines they took, and how much vitamin E they had in their diets. The researchers examined each person, measured their height and weight, and then followed their medical records to see if they developed Parkinson disease. They kept track of these people for about 9.4 years.

What were the results of the study?

The researchers found that 87 people developed Parkinson disease. They found that women who had hadhadhigh levels of total cholesterol in their blood were less likely than those with low cholesterol levels to develop Parkinson disease. The findings did not change even when the researchers considered the role of other factors, such as smoking, Vitamin E, coffee, height and weight, presence of the *APOE* genetic marker, and the use of drugs to lower cholesterol. When the researchers looked at cholesterol levels and the risk of developing Parkinson disease in men, they did not find a relationship.

The researchers are not able to clearly state why the difference exists between men and women in their finding, but their theory is that it might be related to a stronger link between levels of coenzyme Q10 and cholesterol in women than in men. Their other theory is that the differences may be related to the effects of estrogen on cholesterol and other fats.

What ***did the researchers conclude?***

They believe that "these results call for further research on the relation among cholesterol, coenzyme Q10, and the risk of [Parkinson disease]."

Because of the relationship between high levels of cholesterol and an increased risk of having a stroke and developing heart disease, researchers are not recommending that people purposefully try to raise their cholesterol levels to lessen their risk of developing Parkinson disease.

Dopamine*: Dopamine is a chemical that is known as a neurotransmitter. Neurotransmitters help relay messages from one nerve cell to another. Dopamine is especially important in relaying messages about movement.*

Mitochondrial dysfunction*: Mitochondria are the main energy source of cells. Mitochondria convert nutrients into energy and also perform many other specialized tasks. Dysfunction means that something is not working or functioning in the correct way. Therefore, mitochondrial dysfunction refers to a situation in which the mitochondria are not working properly.*

Oxidative stress*: Oxidative stress is a process in which substances called free radicals build up in the cells as the cells convert nutrients into energy. The free radicals damage different parts of the cells in a process that is similar to the way in which rust builds up on metal. The free radicals can be counteracted by antioxidants, but if your cells do not have enough antioxidants, the free radicals accumulate and cause damage. Coenzyme Q10 acts as a scavenger of free radicals.*

{What follows is an example of what you will get if you go to http://www.pdtrials.org/ . It is THE place to go to find out what trials are available. There are also up-to-the-minute

articles about PD, and lots more. Take a look. Stan}

PDTrials.org

Welcome to PDtrials.org where you'll find up-to-date information on Parkinson's disease clinical trials currently enrolling participants in the U.S. by symptom and location, as well as the latest news and views on what's happening in the world of Parkinson's trials.

If you are a researcher or someone in the medical field who would like to share information about a Parkinson's disease clinical trial through this website, you may do so free of charge. Learn more.

PDtrials.org is the website of the PDtrials campaign, an initiative of the major Parkinson's patient voluntary groups to accelerate the development of new treatments for the disease.

New Trials

==NET-PD LS-1 Creatine in Parkinson's Disease - Recruiting 1,720 Participants!.....*read more* 04/23/2007

==Risk Factors for Progressive Supranuclear Palsy (PSP).....*read more* 04/23/2007

==Parkinson Associated Risk Study (PARS): Evaluating Potential Screening Tools for Parkinson's Disease.....*read more* 04/10/2007

==Study of CERE-120 in People with Parkinson's Disease.....*read more* 04/10/2007

==Study of the Effect of Long-Lasting Sequence Movements in Early-Stage and Advanced Parkinson's Disease.....*read more* 04/06/2007

==A Study of a New Drug, Azilect, Alone or in Combination Therapy for Parkinson's Disease.....*read more* 03/05/2007

==Safety Study of Gene Transfer Therapy in People with Parkinson's Disease.....*read more* 03/02/2007

==A Study to Compare an Implant with Sensory Training for Improving the Ability to Swallow in Chronic Dysphagia.....*read more* 02/05/2007