Connecticut Parkinson's Working Group Newsletter July 2000

Clinical Trials

Jackie Dorwin

"Clinical research trials." This phrase sounds so imposing. What is an ordinary fifty year old mother of three doing in one? It all started when my PD had progressed to a point where my neurologist suggested a consultation at the Yale Movement Disorders Center. The usual motor and neurological tests were done, some questions and then an evaluation. I thought that that was it, when the director of the Center joined the examining doctor and me and brought up current research, potential for a cure, and how I might become involved. Was this something I wanted to do? After we discussed the commitment, risks, and clinical trials in general I agreed. That was all there was to my getting involved in the fight to find a cure for PD.

The decision has been one of the most satisfying I have ever made. However, participating in a clinical trial is not for everyone. In a clinical trial a new drug is taken to see how your body reacts. Of course no one knows exactly what will happen (that is the point of the trial) and there might be risks. I think of the guinea pigs in the past who took levodopa, thank them for sinemet, which has so improved my life, and applaud their courage. Then I think of my children: If one of them got PD would they benefit from my research participation? Since I believe that I should do what I can for as long as I can, I will do clinical trials even though my situation is, as is true for everyone with PD, deteriorating.

The FDA prescribes the steps to bring a new drug to market. This process can go on for 15 years and cost as much as $500 million. A typical case goes something like this: A research team develops a drug which they believe will benefit PWP; Animal tests are done to determine safety and efficacy; tests on humans are done. It may end at any stage if the drug proves dangerous or is not effective. The tests on humans are called clinical trials. Phase I involves fewer than 100 normal, healthy people to test the drug's safety. Phase II utilizes several hundred volunteers who have the disease to test the drug's effectiveness. Phase III can involve several thousand people with the disease and evaluates, among other things, side effects. Frequently this phase is a double-blind, where the patient is given either a placebo or the real thing, no one knows which.

Even if these steps are successful, the process is not over . The pharmaceutical company proceeds with a New Drug Application and the FDA scrutinizes the drug and the research process in its entirety. Approval of the new drug means that it can be prescribed by physicians, but the studies don't end there. The company continues to submit reports to the FDA, and occasionally a Phase IV study is required.

Each clinical trial has its own participation criteria: Some want newly-diagnosed and as yet unmedicated PWP; Some want those who are only on sinemet; There may be restrictions on the length of time you have had your PD; There may be a certain symptom they are trying to target, so you must have this symptom. You must be able to follow directions and be available for appointments at specific times. An Informed Consent Form must be signed by you and witnessed; you are free to withdraw from the study at any time.

And then there are the tests. All trials start with a basic neurological exam. For the finger-tapping, toe-tapping, walk-and-turn wizards that we are, this establishes a baseline from which progress can be evaluated. Blood work, EKG, urinalysis, and sometimes a cognitive function test are done. (I've pretty much memorized counting backwards from 100 by 7, and I can easily list five items in a store that begin with the letter "b").

After these preliminaries you are into the trial. The drug is dispensed with instructions about how and when to take it. Most trials require diary-keeping, and have a schedule of appointments when you are monitored. In the past two years I have participated in three clinical trials, all with their own quirks. I'm still waiting for a patient evaluation form that allows me to comment on one study. In another the medicine was packaged with no regard to the fine motor skills of the participants. (I couldn't get the pills out of the blister pack!). In a third the company said that the pill, which was dissolved sublingually, tasted like chocolate. If that's what chocolate tastes like, Hershey would have been out of business long ago!

Over the course of the clinical trial you become acquainted with the staff at the Center, and get a real feel for the intricacies of the endeavor. The staff must travel to discuss the research and the trials, learn how to administer the trial, keep volumes of paperwork, make arrangements for appointments, give tests, and ask time after time "How are you feeling compared to two weeks ago?" It is a wonder that they manage to keep their good nature through it all.

Choosing to participate in a clinical trial is not for everyone. There are risks involved, and benefits. The whole subject is covered thoroughly on the National Institutes of Health web site http://clinicalstudies.info.nih.gov or you can call 800-411-1222.

MOVERS AND SHAKERS OF NEW ENGLAND

is a support group for young onset people with parkinson's and their caregivers that covers the whole of New England. They meet the first Saturday of each month (except for July and August) from1 :00 PM to 3:00 PM at the UMASS Medical School in Worcester, MA., Room S1-123. The current monthly meeting notice can be found on the computer at http://members.xoom.com/msneweb/msne. Rick and Melissa Doppler are the co-founders of the group, and they are available for phone support calls with either patients or caregivers who may be having trouble coping, and will also give you directions to the meeting. Their telephone number at home and for the group is 978-929-9295.

Pill Poppin' Blues.

Gunilla Norris

Each morning my partner and I take a pile of pills. He is a PWP and I have a tricky digestive system. Between us it seems we consume a pharmacy worth. No fun! One morning as I was seeking quiet and introspection this little blues song popped up. I tried to make it go away but it kept up its little riffs. Here is the Pill Poppin' Blues.

For your ills,
take your pills

In pity do not wallow
just swallow, swallow, swallow.

Delay is no use,
it's just abuse.

Procrastinate, you silly billy
you have to take them willy nilly.

Pop them in now
One, two three.
Soon you'll forget this
and be free.

If this process
you with horror fills,
just squint and bear it.
Take your pills!

Glug and glug,
the water pour.
Open wide
and swallow more.

We know it kills.
Just take your pills !!!!

From the editor ---

We have a new name but are really a continuation of what was, from 1994-1996, Connecticut Young Parkinsonians. The word "Young" was wrong since we were a group comprising all ages; our defining trait was that we all wanted to work to help each other, to help the PD research community get funding, to help doctors develop new treatments and to address issues that local support groups

often don't such as the problems of young onset PWP and caregivers CG(or carepartners). Hence the new name. Our goals are the same.

Our meeting in Waterbury this April, sponsored by Dupont Pharma, brought together 60 of us. We heard from Dr. Mohammed Hassan who gave an animated and thorough overview of PD and current research. We had a great hour of discussion touching on many topics of common concern; the consensus was that discussion should be the backbone of all meetings. Most attendees felt that we should meet three or four times yearly, on weekends and at a central location. July was chosen for our next meeting.

The emphasis of previous newsletters was on the experiences and activities of group members; this will continue. Anyone who has a topic to discuss should let me know about it, and I have no qualms about approaching people to contribute articles. There will usually be brief notes on significant news to PWP gleaned from the many sources reporting on Parkinson issues. We will often hear from members of the medical profession.

Jackie Dorwin and I are meeting facilitators; but the meetings and newsletter are the result of a group effort, so everyone should make an effort to participate to the best of his or her ability. Participate in clinical trials; write to and visit your representatives in congress to push for PD research funding, help others in the group who need information or an understanding ear and spread the word that we exist. You know, we are a focus for others in the state, and nearby states, who are involved with PD in one way or another - doctors doing research, pharmaceutical companies with new products, and most importantly PWP and CG who need the support of others in the same boat. ***Stan Wertheimer***

CONNECTICUT PARKINSON WORKING GROUP MEETING 22 JULY 2000

at the Connecticut Valley Hospital, Middletown **from** 1 PM -> 3 PM

We will hear from a representative of the ***Yale Movement Disorders Clinic*** about opportunities to participate in present and future clinical trials they are doing. Our guest speaker will be James O'Malley, PhD ***Pfizer Central Research*** who will discuss stem cells, what they are and how they might play a part in treatment and cure of Parkinson's Disease. There will be lots of time left for general discussion and also a breakout session for caregivers in another room.

We will meet in the Norwich Room (2nd floor) of Haviland Hall on the CVH campus. It is air-conditioned, has comfortable seating at tables, is accessible to all and there is a snack shop in the same building. Drinks are graciously being supplied by Brian Clark. Our benefactor at CVH is Al Michaud, Chief of Rehabilitation Therapies.

To get there: Take route 9 to exit 12, from north or south. From the south: turn right at the end of the exit ramp onto Bow Lane and make an almost immediate left onto Harvey Drive. From the north: cross back over route 9 and follow directions above. The parking lot borders Haviland Hall, which is to the right of a large A frame chapel. If you need wheelchair access, there is a dropoff in front of Haviland Hall.

We would like to have some idea of how many attendees there will be. Please fill out the following and send it to **Jackie Dorwin, 132 Highwoods Drive, Guilford, CT 06437**, call her at **203-453-2655** or send an email to jdorwin@aol.com . Of course, it is not necessary to do this to attend - just come along. Please let others in your support group know of the meeting.

NAME(S)_____

ADDRESS _____ TELEPHONE _____

_____ EMAIL _____

_____ NUMBER IN YOUR GROUP:

Newly Diagnosed

Tim F.

When I was first asked to write this article I readily agreed. Then I thought, "Tim, you could probably right a book if you wrote down every detail of recently being diagnosed with Parkinson's Disease." I decided to focus on my emotions during the time period of testing and post diagnosis.

During the summer of 1999 I was admitted to the hospital for chest pains. Before being admitted my wife mentioned to my general practitioner that my essential tremors had taken a turn for the worse. He suggested after I get out of the hospital I should see a neurologist. Well 6 months later with complaints of weakness, clumsiness, and terrible tremors, I finally went to a neurologist who after an MRI diagnosed me with mild cerebellar ataxia. My wife, the nurse, was not happy with that diagnosis so she made an appointment with my current neurologist. After many vials of blood, several CAT scans, an EMG, and finally a trial run of Sinemet®, I was diagnosed on February 10, 2000.

My wife and I had worried about the worst as they ruled out disease by disease. She made a good point when she said, "At least you won't die in a few years." That wasn't comforting at the time. I was angry and sad. Why should I get this "old person's disease"? Everyone that came in to my pharmacy with Parkinson's was 60 years or older. The tremors, ataxia, and bradykinesia associated with the disease were not only interfering with my day to day activities but they stopped repairs on the "fixer upper" of a home we bought in January.

Depression and anxiety took control of my life when the Parkinson's didn't. My neurologist added Zoloft to my regimen of amantadine and selegiline. I attended our meeting in Waterbury while on this medication. I had gone from unilateral symptoms to bilateral symptoms. I was quiet and withdrawn. The Parkinson's was worsening. Our next trip to the neurologist ended up with him taking me off Zoloft and I returned to my unilateral symptoms.

At the same time something popped into my head – "Why was I going to let this disease run my life? Why couldn't I just take advantage of the good days and shrug off the bad days?" My whole family was understanding of my sudden nap attacks and the fact that sometimes I just was quiet because I didn't feel well. My wife Siobhan was supportive all the way looking up research on the Internet and contacting support groups.

Another turning point was the death of my mother. She was diagnosed with cancer and died 18 days later. One month earlier she was golfing in Florida with my father. She would have wanted me to be strong for my family's sake and I would make sure I was

I decided to grab what I could while I can. I took a job promotion that proved to be more stressful than anticipated. When I can't sleep at night I "surf the net". My twelve-hour days as pharmacy manager take their toll on me so I relax on my days off and enjoy my children. I even recently helped my brother-in-law put an addition on our house. My wife kept asking if I was OK – I was having fun even if I did have to take a few breaks.

I have come to accept my Parkinson's Disease thanks to my wife's words of wisdom. Things could be worse – my children or wife could be sick or I could have a fatal disease. I have much to be thankful for – especially my friends and mostly my wife and children. Parkinson's is now just a roadblock in my life. Something that gets in the way but it will never take away my life with those I love.

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Thanks

to Donna Diaz and Gladys Tiedeman of the APDA here in Connecticut for their continual help and support of our efforts to bring this group, CPWG, together. It is safe to say that we could not have done it without them.

Source: University Medical Center St. Radboud, Nijmegen, The Netherlands.
22 March 2000. THC 346 stops symptoms of PD in monkeys.

Two neurobiologists from Nijmegen (the Netherlands) have found the compound THC 346 to stop the progression of PD in monkeys completely. Within 3 months a trial will start with PWP. The medicine might also have a positive effect upon ALS and Alzheimers. One of the researchers, Prof. dr. A. Cools of the University Medical Center St. Radboud, said the discovery to be every researchers dream. He and his collegue Andringa could not believe it when they saw the effect of THC 346 in tests with rhesus monkeys. Worldwide researchers never before succeeded in actually stopping the progression of PD, Cools said.

The neurobiologist stressed that the compound does not cure PD. Symptoms that already appeared, will stay. But if PWP have their first symptoms, these symptoms are still minimal. Until now therapy was often delayed because of severe side-effects of the available medication. THC346 makes it possible to stop the progression in an early phase at a level that people still can function quite normal.

Goetz C et al; Neur 2000;54:710-714:
Authors examined 105 early-stage PD patients in the placebo group of a controlled trial of ropinirole(Requip) and found that 16% of them experienced improvement of PD symptoms.

Schumacher J et al; Neur 2000;54:1042-1050:

To test safety and efficacy of unilateral embryonic pig cell transplants in PD patients, they followed 12 recipients for a year. They found variable but general improvement in symptoms, no porcine retrovirus and no serious adverse effects.

Science News, 25 Mar 2000;197(news item):
Some details about the pig cell transplant trial cited above: In this first trial to establish safety, a relatively small amount of tissue was used. Nevertheless, symptom improvement was "dramatic" in 3 of the 10 advanced-PD subjects, moderate in 3 others, while the remaining 4 were unchanged. A new study with 18 subjects, using 4 times the former amount of tissue, includes a control group getting sham transplants (at first).

Australian Team Reports Stem Cell Breakthrough By Wendy Pugh
MELBOURNE, April 4, 2000 - (Reuters) - Australian scientists said on Tuesday they had succeeded in developing nerve cells from early human embryos (stem cells) which could lead to a cure for Parkinson's disease and a range of other health problems.

``We hope that one day we will be able to produce pure populations of specific types of nerve cells that could be used for screening new medicines or for transplantation to correct specific diseases,'' senior research fellow Martin Pera said. ``So for instance, if we made dopamine-producing nerve cells, those can potentially be used to treat Parkinson's disease.''

From: Jeff Jones <jpjones@BIGFOOT.COM>
Subject: Care Web Pages
It has taken me a healthy group of time to "complete" the CARE Web Pages. The CARE Web Pages are as complete as any group of pages that continue to be updated. What is CARE? CARE (Caregivers Are Really Essential) is a sublist of the main PD list, which is especially for caregivers (CGs) of Parkinsonians (PWPs). The CARE Web Pages are a group of pages drawn from information shared in messages to the CARE List. There are links to other parkinson or CareGiver resources. The URL is: http://www.crosswinds.net/~caregivers/index.html

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New drug safe for Parkinson's, but not effective by itself

NEW YORK, Apr 24, 2000 (Reuters Health) - Remacemide, a new type of drug for treating Parkinson's disease, has few side effects, but it does not improve the symptoms of the disease when used by itself, according to preliminary findings. However, researchers in the Parkinson Study Group are hopeful that the drug might be effective when combined with levodopa, the drug most commonly used for Parkinson's.

"If ongoing studies confirm that remacemide used in conjunction with (levodopa) improves patients' symptoms, it may be the first of a new class of Parkinson's therapies," said Dr. Steven Schwid, a member of the study group from the University of Rochester, New York, in a news release. "Based on its favorable safety profile and several animal studies, further studies of remacemide are warranted as symptomatic therapy in levodopa-treated patients and as a neuroprotective agent," Parkinson Study Group concludes.

Zesiewicz T et al; Mov Disord 2000;15:305-308:

Open-label test of sildenafil citrate (Viagra) in 10 male PD patients showed significant improvement of sexual function.

Eskandar E et al;J Neurosurg 2000;92:375-383:

Two-year followup of 75 successive recipients of unilateral pallidotomy, guided by MRI and macrostimulation but not microelectrode recording, showed the protocol to be safe and effective treatment for advanced-stage PD.

Bejjani B et al;J Neurosurg 2000;92:615-625:

They report 12 advanced-PD patients who received bilateral subthalamic neucleus stimulation implants guided by stereotactic MRI, macrostimulation, and electrophysiological guidance [microelectrode recording]. At 6-month followup, all showed varied but generally good results.

In-Home Pesticide Exposure Increases Parkinsonís Risk

SAN DIEGO, CA Pesticide use and exposure in the home and garden increase the risk of developing Parkinsonís disease, according to a study of almost 500 people newly diagnosed with the disease. Researchers announced their findings at a presentation at the American Academy of Neurology's 52nd annual meeting in San Diego, CA, April 29 May 6, 2000.

"This study is the largest yet of newly diagnosed individuals with Parkinson's disease and it is the first study to show a significant association between home pesticide use and the risk of developing Parkinson's disease," said study lead author Lorene Nelson, PhD, a neuroepidemiologist at Stanford University School of Medicine. The preliminary results from this study mirror what is already known about the increased risk of Parkinson's disease associated with occupational exposure to pesticides.

Histories were compiled of 496 people who had been diagnosed with Parkinson's disease about past use of pesticides. The Parkinson's patientsí lifetime histories were then compared to 541 people without the disease. Researchers found that people who had been exposed to pesticides were approximately two times more likely to develop Parkinson's disease than people not exposed to pesticides.

Academy of Neurology Web site: http://www.aan.com. For online neurological health and wellness information, visit NeuroVista at http://www.aan.com/neurovista.

AAN: Viagra (sildenafil) may reduce levodopa-induced dyskinesia in Parkinson's patients

SAN DIEGO, CA -- May 3, 2000 --Sildenafil (Viagra) may provide a novel treatment for motor complications in late-stage Parkinson's disease, according to a study presented at the 52nd Annual Meeting of the American Academy of Neurology held here May 2, 2000.

While levodopa is the most effective medication for Parkinson's disease,its long-term use leads to dyskinesias, or abnormal uncontrolled movements, in more than 50 percent of patients within five years.

David Swope, MD, a neurologist at Loma Linda Medical School, has begun to gather evidence that sildenafil may be an effective treatment for dyskinesia. Dr. Swope treated eight PD patients, five men and three women, with open-label sildenafil for moderate-to-severe peak-dose dyskinesias. Each patient received 25 mg of sildenafil on two consecutive days in addition to their previously optimized anti-parkinsonian medications (including amantadine, an antiviral drug with some antidyskinetic effects). Five of eight patients reported improvement, with three reporting complete resolution. One of three non-responders went on to try 50 mg, with noted improvement at the higher dose. All responding patients reported benefit for the entire day, with dyskinesia returning after treatment was discontinued. No patient reported worsening of parkinsonian symptoms, and several reported improvements.

Caffeine May Prevent Parkinson's **by LINDSEY TANNER, AP Medical Writer**

CHICAGO, May 23, 2000 (AP) - An intriguing new study suggests coffee may prevent Parkinson's disease. How a product that makes people jittery could keep them from getting a disease that gives them tremors is a paradox not examined in the study of 8,004 Japanese-American men in Hawaii. The researchers said the benefits are probably due to caffeine - apparently the more, the better. Outside experts said that if the findings hold up, they could lead to ways to treat PD more effectively or even prevent the disease.

The study found that men who didn't drink coffee were five times more likely to develop PD than those who drank the most - 41/2 to 51/2 6-ounce cups a day. Non-coffee drinkers were two to three times more likely to get the disease than men who drank 4 oz to four cups a day.

Ross said it is possible that heavy coffee drinkers have a brain composition that may make them resistant to PD. Previous studies have found low rates of Parkinson's in "thrill-seeking" people who tend to engage in high-risk behavior like smoking and heavy drinking, and heavy coffee drinking also fits that personality profile. However it is too early to recommend coffee as a treatment.

The latest issue of SPRING's newsletter includes articles on: Stem Cells; PDS Medical Advisory Panel meeting; Medical Research Funding; Parkinson's Disease Nurse Specialists.

SPRING is the Special Parkinson's Research Interest Group), the official Special Interest in the Parkinson's Disease Society of UK. http://spring.parkinsons.org.uk/SPRING_Times/

Gene Linked to Early-Onset Parkinson's Disease

NEW YORK, May 26, 2000 (Reuters Health) - Mutations in the parkin gene can cause Parkinson's disease to develop early in life, but the symptoms of this early-onset form of the disease do not differ from the later developing illness.

Parkin gene mutations have only recently been linked to Parkinson's disease in younger individuals, so the frequency of the mutations and the manifestations of this form of the disease have not been studied previously, according to Dr. Christoph Lucking from Hopital de la Salpetriere in Paris, France and an international team of researchers.

The authors studied 73 families with early-onset, inherited Parkinson's disease (including 152 affected family members), as well as 100 other patients whose early-onset Parkinson's disease did not appear to be inherited.

Nearly half of the families with early-onset Parkinson's disease (PD) showed mutations in their parkin genes, the authors report, whereas 18% of the patients with isolated early-onset PD had parkin gene mutations. In both groups of patients, two abnormal parkin genes appeared to be required for PD to develop. Geneticists called such diseases autosomal recessive, meaning that an affected gene is inherited from each parent.

Patients who carried abnormal parkin genes were younger when their disease developed, and they were more likely to show abnormalities in muscle tone and reflexes than their normal-parkin-gene counterparts, the report in the May 25th issue of The New England Journal of Medicine indicates.

Once PD developed, patients with parkin gene mutations were more likely than those without mutations to improve with medical therapy, the researchers note, although they were also more likely to experience side effects from the drug levodopa.

Despite these differences, the investigators suggest, physical examinations and symptoms were not specific enough to be able to distinguish patients with mutations from patients without mutations.

A wide variety of parkin genes was detected by specific testing, the researchers say, but a relatively simple screening test should detect 70% of the parkin mutations that cause Parkinson's disease.

"Mutations in the parkin gene are a major cause of early-onset autosomal recessive familial Parkinson's disease and isolated juvenile-onset Parkinson's disease (at or before the age of 20 years)," the authors conclude.

The results also suggest ``...that among patients who are older than 30 years at the onset of isolated (that is, not familial) Parkinson's disease, the disease is mainly due to causes other than parkin mutations,'' the authors add.

SOURCE: The New England Journal of Medicine 2000;342:1560-1567.

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DISCLAIMER: Articles in this newsletter is for information only. Any questions of treatment should be discussed with your physician.

WRITE! your representatives in congress. Christopher Dodd, Russell Senate Office Building, Washington, D.C. 20510. Joseph Lieberman, Hart Senate Office Building, Washington, D.C. 20510.

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