Connecticut Parkinson's Working Group Newsletter

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A FRESH ASSAULT ON PARKINSON'S

By Michael Arndt; Edited by Adam Aston

Last Fall, Amgen abruptly halted tests on a PD treatment—a protein-based drug known as GDNF—because animal studies indicated it could cause permanent harm to humans. Now scientists at biotech startup Ceregene think they may have found an alternative: a growth factor called neuturin that is a first cousin of GDNF.

Ceregene researchers have begun a yearlong study of 12 advanced-stage PD patients at the University of California at San Francisco and Rush University Medical Center in Chicago. Each patient received four injections of a genetically modified virus designed to deliver therapeutic genes to the brain.

The researchers hope that the drug, developed at Washington University in St. Louis, will revive dopamine-producing nerve cells that are needed for smooth bodily movement but that are destroyed by the progressive, crippling illness. In earlier tests of neuturin on primates, tremors began diminishing within three months, says Jeffrey Ostrove, Ceregene's CEO.

The McGraw-Hill Companies, Inc. Business Week, Oct 10, 2005 i3954 p79

FUND RAISING REMINDER

CPWG has just kicked off its 2nd annual fund raising campaign. All Newsletter recipients should have received a request letter. Please be as generous as you can or better yet suggest to those on your Holidays list that you would prefer a donation in your name to CPWG. Remember that we are an IRS recognized charitable organization so all gifts are tax deductible. Checks should be made payable to CPWG and mailed to:

CPWG
Stephen Holahan, Treasurer
20 Franklin Lane
Glastonbury, CT 06033-3009

AVOIDABLE CAUSES OF DBS FAILURE

It should be mentioned that WE MOVE is solely supported by Medtronic Corporation, the only makers of the implant devices. It is good to have the results of this article; they not only represent a "caveat emptor" but an implied vindication of any problems with the equipment.

Why is this study important?

In 1997, the FDA approved the use of deep brain stimulation (DBS) for the treatment of PD and essential tremor and, in 2003, also approved the use of DBS for the treatment of dystonia. Since that time, thousands of people have had operations for the placement of DBS electrodes and stimulators. At first, most patients were treated at centers that specialize in the treatment of movement disorders. However, as more surgeons have learned how to implant the electrodes, and more neurologists have learned how to program them, the operations are now being performed at less-specialized centers. Currently, there are no consensus-approved guidelines for the

- Selection of patients who are most likely to benefit from this treatment
- Training of surgeons who implant the electrodes
- Training of personnel who program the stimulators
- How, when, and where the programming takes place
- How to educate patients and physicians about complications
- How the complications should be managed

What was the purpose of the study?

The researchers hoped to be able to improve the treatment of dystonia, PD, and ET with DBS by studying a series of patients who have had less than favorable results after their operations for placement of DBS leads and stimulators. "Favorable" was defined as being able to decrease the amount of medication that was required before the DBS operation and maintain the same level of functioning.

Who participated in the study?

Over two-years, 41 patients who had had their operations elsewhere were evaluated at one of two movement disorder centers: the University of Florida or Beth Israel Medical Center in New York. All of the patients were having problems with DBS treatment for PD, ET, or dystonia. Neurologists and neurosurgeons who specialize in the treatment of movement disorders at both of these institutions examined the patients, their medical records, and the DBS leads and stimulators.

What were the results of the study?

The most important factor in predicting outcome of treatment with DBS is proper patient selection. In 32 of the 41 patients, the specialists agreed with the diagnosis that had been made before the operation. In nine patients, the diagnosis was changed. In five patients, a condition was diagnosed that would not have been expected to benefit from DBS.

Thirty patients had seen a movement disorders specialist before the operation. Fourteen patients had neuropsychological testing before the operation. Five patients did not take the correct medicine for a long enough period of time before the operation to determine whether or not the medicine was effective. Five patients were also found to have had severe problems with thinking clearly (cognitive impairment) before the operation.

Nineteen of the 41 patients had the DBS leads in the wrong place. When the surgeons at the University of Florida or at Beth Israel Medical Center replaced the leads, seven of the patients had marked improvement and three others had partial improvement (defined as symptom improvement but not to the level expected by the researchers). Three patients had problems with the batteries in the neurostimulator, two had infections, and one had a broken lead.

Seven patients had no access to programming for their stimulators—two because they moved and two because their doctors moved. Eight more patients had had their operations at centers far from their homes, and they had trouble finding a device programmer who was near them. In 15 patients, programming appeared to be inadequate. The specialists were able to reprogram 51% of these leads, but the sessions took almost twice as long as normal. Thirty patients required one or more medication changes.

After being treated by movement disorders specialists at these two centers, 21 of the 41 patients in whom DBS had been previously determined to have "failed" had good outcomes. In addition, another six patients had modest improvement.

What was the authors' conclusion?

"This study highlights the important point that all of these complications were potentially preventable. As more DBS is performed, practitioners will need to be aware of the timeline of preventable problems, which may include failures of triage, screening, surgery, and postoperative follow-up . . . This case series provides important insight into the common reasons for 'DBS failures' and proposes some effective strategies for their management."

Okun M, Tagliati M, Pourar M, et al.
Management of referred DBS failures. A retrospective analysis from 2 movement disorders centers, *Arch Neurol* 2005;62:1-6.
From *WE MOVE News,* November 17, 2005

INTERVIEW BY JEFF LINCOLN WITH DR. JOHN SEIBYL—PART 2

This is the second half of a two part interview by Jeff Lincoln (JL) with Dr. John Seibyl, (JS) the President of Molecular NeuroImaging (MNI) and the Executive Director and Senior Scientist for the Institute for Neurodegenerative Disorders (IND). During the first installment, Dr. Seibyl described his personal story and how he came to be at IND/MNI. During this second installment of the interview, we will explore what happens during a SPECT Scan, the type of brain scan used by IND to evaluate a patient's progression through the stages of Parkinson's Disease (PD).

JL: I want to go on now to talk about magic, but I also want to put it in some way such that people who are not technical can still get something out of this article. Let's start by asking what happens from the beginning of the scan.

JS: We use a radioactive material called Iodine123-BetaCIT. We make this medication here at IND. A laboratory upstairs receives the radioactive Iodine from Vancouver, British Columbia We have a chemist whose specialty is hooking the radioactive Iodine onto our medication.

JL: How long does this medication last after you make up a batch?

JS: Like all medical isotopes, it has what is called a "half life". This is the time it takes for 1/2 of the radioactive molecules to decay. For Iodine 123 the half life is about 13 hours

JL: Thanks. Let's continue.

JS: When a research participant comes to IND, he/she gets an injection of the radioactive medication and then leaves. He/she comes back the next day because it takes time for the medications to accumulate in the areas of the brain we are interested in imaging. During the time after the injection but before the scan, the medication travels through the bloodstream and is taken up by the brain, where it accumulates near the dopamine producing cells. When these cells die in people with Parkinson's Disease (PWP's), we don't see as much of the radioactive Iodine taken up into the brain. Once the medication is taken up into the brain, it stays near the dopamine neurons while undergoing radioactive decay. This decay is captured by our "camera" [the large instrument that actually does the scan!—ed.] The camera takes pictures from all different angles to collect information on where the decay is coming from in the brain. We then take that two-dimensional data and process it to make it a three-dimensional image. We can rotate the image, slice it, do all sorts of other things, but the most important thing we can do is to get a number that corresponds to the number of dopamine neurons in the brain. That number is important, because a PWP may lose 6–8% of these sites over a year. Normal people might lose 0.3% sites per year. That's how we use the imaging. It sounds like a bit of magic.

JL: For people in the GPI 1485 study, there are 4 scans: one before starting the study and then at 1 year, two years and for me at 3 years

JS: The end analysis that for each of those scans is a number that we call an "uptake" ratio and we look to see how that number changes from the first to the last scan.

JL: Do you have 2 numbers, one for each side.

JS: We get four numbers, two on each side corresponding to 4 areas of interest.

JL: I think we can skip the details. How long have you been doing these larger studies?

JS: I started developing this methodology in 1992. It took us about 4 to 5 years of research to get the test as simple as it is today. Originally we weren't sure how to get that uptake number. We tried all sorts of things: long studies, imaging patients over and over, day after day. We studied scans from different days to see if we got the same results. We needed a reproducible scan. Eventually we published our results. It took a lot of work before we found the methods to do large studies effectively. That said, we actually started doing these large studies about 8 years ago.

JL: What's happening in Europe?

JS: Dr. Marek and I created a consortium of movement disorder specialists in Europe who have interest in imaging. We called ourselves the Amadeus Consortium because our first meeting was in Vienna, Austria, near Salzburg—the birthplace of Mozart. We are now in eleven sites in five different countries. We had to develop techniques for getting data from different cameras. These involve me going to Europe to calibrate multiple machines. Scans magically come back to IND over the Internet and we analyze these at this lab. We now have well-established consortium of investigators to do further studies in Europe. It's been great fun. We've created a lot of international good will.

JL: Do you do more than study PD?

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JS: We do studies in non-Idiopathic PD disorders. We've looked at them from an imaging perspective. Could we use an imaging test to differentiate PD from similar non-PD disorders? The answer is yes and no. We also have done some studies in Alzheimer's Disease, trying to develop some imaging techniques keying off the techniques we have developed in PD.

JL: What about stem cell research?

JS: We don't have the capacity to do stem cell research here at IND. I think this is an interesting and potentially valuable technique. There is a long way to go. There has been a lot of hype in the media. We might be involved in the future in imaging stem cell research subjects to assess the integrity of their introduced stem cells.

JL: If you look five years from now, what do you see?

JS: What I see as the hot new area in PD treatment are the medications that modify the course of the disease. Five years ago I was skeptical of this approach. The fact is that right now there are human trials under way or soon to be underway of about 14 different approaches for arresting or slowing down the progression of PD. That's remarkable. What is so interesting is the different targets for these studies hitting different mechanisms of PD. I am as confident as a skeptical research scientist can be that something is going to hit. That would represent a whole new way to think about treating PD. These approaches don't just apply to PD. They also apply to Parkinsonism, Alzheimer's, etc. There are some neat ideas. Most of these will not pan out, but this is a vibrant active area of research. It's fun to be able to participate in a small way in these studies. The most gratifying thing about doing this kind of work is that it is connected to people's lives. I am completely convinced that the work coming out of IND and MNI is affecting the way clinicians are thinking about treating PWP's. This is an immensely gratifying place to be in partnership with our patients.

JL: I think we'll end on that note. Thank you for your time . . .

The following pinpoints an area that we could be more active in. We did help out a few years ago with IND recruiting of people for clinical trials; at present we don't have an organized effort.

MAJORITY OF PHYSICIANS WHO TREAT PD DO NOT REFER PWP TO CLINICAL TRIALS

- **Low Awareness Seen as Major Barrier to Clinical Trial Participation**
- **PD Patients Lack Information but Cite Support Groups as Primary Source of Data**
- **Groups Join, Create Education Campaign, Web site *www.PDtrials.org* to Address Issues**

NEW YORK, June 14, 2005—While almost all (above 96%) of the MDs in the US who treat PWP agree that clinical trials are necessary to find better treatments for the disease, the majority of MDs have discussed clinical trials with just 10% or less of their PWP (65% of neurologists and 54% of primary care MDs/gerontologists) and have never referred a patient to a clinical trial (53% of neurologists and 83% of primary care MDs/gerontologists). These are among the highlights of a recent nationwide survey commissioned by The Michael J. Fox Foundation for PD Research and conducted by Harris Interactive® on behalf of the Advancing PD Therapies (APT) campaign.

Major Findings

The survey found that knowledge and opinions among U.S. PD patient closely mirror those of MDs. Almost all (95%) of the PWP surveyed agree that clinical trials for PD are necessary to find better treatments, yet only 11% report that their MD ever suggested that they participate in a trial. At the same time, those PWP surveyed who are aware of trials cite support groups (40%) and other PWP (27%) as the most common sources of information about trials—only 11% cite their MDs.

Lack of adequate information about clinical trials was identified as a barrier to clinical trial enrollment. Only 14% of primary care MDs, 21% of neurologists and 18% of PWP surveyed indicated that they are somewhat or very satisfied with the amount of information available about clinical trials for PD.

"People are not getting the information they need to make decisions as to whether to participate in a trial," said Michael J. Fox. "The fewer people who go into trials, the longer it will take to develop new treatments. To meet this challenge the PD community has initiated a campaign—Advancing PD Therapies—to give PWP and MDs better information."

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APT Launches Online Clinical Trials Resource

The APT campaign has launched *www.PDTrials.org*, a major initiative designed to educate people about the importance of clinical trials, explain how clinical trials work and provide a comprehensive, user-friendly, web-based resource to enable PWP and caregivers to identify and locate appropriate PD clinical trials. The campaign seeks to improve patient-MD communication about clinical trials and provides useful information to help PWP and their MDs determine whether enrollment in a clinical trial is an appropriate option.

Survey Reveals Challenges

The survey results revealed that in addition to dissatisfaction with the amount of information available, MDs and PWP have reservations about clinical trials. Slightly more than half of MDs (52%) agree they would not recommend that a PWP enroll in a trial if their disease is well-controlled. And, while 78% of PWP surveyed indicate that they trust the MDs and scientists who run clinical trials to "do the right thing," 77% believe that if they participate in a clinical trial they may receive a placebo instead of a drug that will help them; 72% expressed concern about continued access to medication once the trial has stopped.

"Most patient concerns can be addressed with specific of education and information," said Robin Elliott, Executive Director of the PD Foundation, the lead organization of the APT collaboration. "For example, individuals may not know that some trials require no more than completing a family history survey or providing a DNA sample. People must also fully understand the informed consent process and the rights it gives them as trial participants. Advancing PD Therapies, through its online resource, *www.PDTrials.org*, provides valuable information that can help empower all the major stakeholders—PWP, caregivers, MDs, researchers and trial sponsors."

Currently less then 1% of PWP are participating in clinical research. This is far short of the level that researchers anticipate will be needed for clinical studies over the next two to three years, including studies of therapies to slow or stop disease progression and to improve symptoms such as tremors. This disparity may result in severe delays in the availability of new treatments that could offer relief for the nearly one million PWP in the U.S.

About the Survey

Harris Interactive® conducted the survey on behalf of the APT campaign with funding provided by The Michael J. Fox Foundation for PD Research, in the United States between January 17, 2005 and March 2, 2005. The MD's survey was conducted online among 500 MDs on the American Medical Association's list of MDs who treat PWP; 250 are neurologists and 250 are PCPs/gerontologists. The patient survey was conducted by mail among 518 adults aged 18 and over with PD. Data from the patient sample were not weighted and are only representative of those PWP surveyed. Data from the MDs sample were weighted to the American Medical Association list of MDs with regard to years in practice, gender and region.

In theory, with samples of this size, one could say with 95% certainty that the overall results for the MDs sample have a sampling error of plus or minus 5% and sampling error for the results of neurologists and PCP's/gerontologists is plus or minus 7%.

Additional Highlights from the Survey

- Of neurologists who have ever referred a PD patient to a clinical trial, the majority (54%) are likely to refer PWP within five years of diagnosis.
- Nearly 80% of PWP surveyed stated that they would be somewhat, very or extremely likely to participate in a clinical trial if one were available in their area.
- Of PWP surveyed, 45% were diagnosed with PD by a neurologist while 37% received a diagnosis from their PCP or family practitioner; 64% of PD PWP surveyed are currently under the care of a neurologist and 40% see a PCP or family practitioner.

About the Advancing PD Therapies (APT) Campaign

Advancing PD Therapies (APT) is comprised of the major PD patient voluntary groups to accelerate the development of new treatments for PD by increasing education and awareness about clinical trials among the PD community. APT is led by the PD Foundation in collaboration with the APDA, The Michael J. Fox Foundation for PD Research, the NPF, the PAN, The Parkinson Alliance and WE MOVE, and is advised by NINDS, the Parkinson Study Group and the Parkinson Pipeline Project.

Visitors to *www.PDtrials.org* can search for a clinical trial by symptom, location, trial type or sponsor and can receive the latest news and views on what's happening in the world of PD trials. Free educational materials, such as a comprehensive guide to clinical trials, can be ordered through *www.PDtrials.org* and the campaign's toll-free number (888) 823–8889.

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WORLD PARKINSON CONGRESS (WPC)

More than six million people around the world suffer from Parkinson's disease (PD). Patients, caregivers, advocates, and researchers are working toward a cure. And for the first time ever, this global community is uniting to share information and hope and to fight PD together.

If you or someone you love has PD, attend the first international World Parkinson Congress and learn firsthand about the latest science and treatments and care for PD. This first-of-its-kind conference for PD will be held February 22–26, 2006, in Washington, DC, and will enable patients and caregivers to

- Meet leading doctors, scientists, and researchers from around the world who will talk about new therapies and next steps in PD research
- Talk with PD advocates and care experts about issues such as stem cell research, clinical trials, coping, and how to afford family care
- Make friends and organize support groups with other patients, caregivers, and families struggling with PD
- Take part in more than 50 different workshops, where you will learn how to
- Manage PD
- Help your children learn how to grow up with a parent who has a chronic disease
- Be a force for health policy change
- Learn how to improve your quality of life through Physical Therapy, Nutrition, Positive Thinking, Art, Exercise, Others

Community session topics include *PD and the Art of Moving, Family Care: The Role of Optimism*, *In Sickness and in Health: Steps to Prevent PD from Consuming a Marriage and a Family.*

To register for the Congress or for more information, go to *www.worldpdcongress.org.*

CPWG REPRESENTED AT WPC

At press time Pat and Tom Sullivan plan to attend WPC. Surely they would like company at the meetings.

In addition, Stan Wertheimer has had one of his pots accepted for their creativity exhibit. The pot, pictured at the right, is a 21 inch vase with a rough copper glaze (green, black, brown.) If you go try to take in the exhibit.

This was published in the UK; it is equally relevant here. As many in CPWG know, we have been actively engaged in meeting with groups of health care professionals to advocate the same actions as outlined below.

PARKINSON'S—GETTING THE TIMING RIGHT.

Chemist & Druggist. **August 20, 2005 p12.**

Access to medication is still a challenge for many with PD, says Robert Meadowcraft. While taking the correct medication at the right time is obviously important for all patients it is absolutely essential for PWP. No two PWP have exactly the same set of symptoms and it is essential that the recommended dosage and timings are followed carefully to achieve optimum symptom control.

Unfortunately, many PWP still report that they are not allowed to self medicate or access their usual drugs at the right time for them in hospital or in care homes. Missing individual dose times or at worst being denied access to medication for several days at a time causes major problems and also increases the challenges for clinical management. A recent study conducted in Sheffield underlined the disturbing findings already reported by patients and their caregivers.

It is therefore not surprising that the Parkinson's Disease Society (PDS) has highlighted improving access to and management of drug treatment as a major campaign priority in 2005.

We want to see improved liaison between the doctors and pharmacists working in hospitals and the GPs and the community pharmacists. A greater understanding of the importance of maintaining the patient's drug regime and ensuring smooth transitions into and out of secondary care is also needed. Self-locking bedside cabinets should now be available routinely for safe storage of medication for those who can self medicate.

Further, the standards set out in the Medicines Management Framework and the recommendations on self medication set out in the Department of Health's Management of Medicines guide (July 2004) should be implemented across the country.

The NSF for Long Term Conditions in March 2005 has an explicit `quality requirement' to improve care in hospital and social care settings and cites PD and medication management as an example where good practice can lead to major improvements in outcomes.

While pressing the importance of improved access to and management of medication within national frameworks and guidelines, we have also developed a learning resource for community pharmacists and their staff to improve their understanding of the impact of PD.

This learning resource is based on an interactive CD which allows them to answer questions about PD after hearing a series of brief interviews looking at aspects of the condition and giving some useful `key facts'. Among the issues covered is an explanation of the symptom fluctuations that are difficult to manage, the `on-off' syndrome where people may suddenly become immobile or have difficulty speaking, and the need to give people time to express themselves without being hurried or placed under stress (which can exacerbate communication difficulties). This learning tool has proved popular and it is planned to revise and update it shortly.

The PDS is keen to work with pharmacists in the community and in hospitals to help them and their staff to improve their knowledge and understanding of PD as a complex, degenerative condition affecting some 120,000 people in the UK for which there is currently no cure. More information is available on *www.parkinsons.org.uk*

JOIN CPWG MEMBER ON A CARRIBEAN CRUISE

Dick and Karen M. are planning a ten day cruise to the eastern Caribbean leaving on February 23, 2006 from New York City. Stops along the way include St. Thomas, Tortola, St. Maarten, Puerto Rico, Great Stirrup Cay, and The Bahamas. The ship is a veritable pleasure palace: it has 2 swimming pools, several hot tubs, a spa and fitness center, cinema, jogging/walking track, library, chapel, and ten international restaurants.

Dick would like others from CPWG to join him. Staterooms with handicap facilities are available, as are rooms with a balcony. If you are interested contact him at 860-663-5640. He can give you cost details (he says the range is $1100-1600 per person, two in a cabin) and who to talk to at his travel agency.

CONNECTICUT PARKINSON'S WORKING GROUP

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DISCLAIMER:

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

Write your Representatives in Congress!

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