



FATIGUE, WEARINESS, AND EXHAUSTION

"I am a 74 year old man. I have had PD for three years. I can live with the PD (not great, but livable), but the fatigue is unbearable. As all my life I was full of superman energy, now I'm good for about an hour or so at a time and between the lightheadedness and the fatigue I'm wasted... I've been told to go and see a shrink and start on anti-depressants. I don't think I'm depressed."

When Dr. James Parkinson mentioned fatigue in, "An Essay on the Shaking Palsy" in 1817, he was describing a patient with end-stage illness. *"The chin is now almost immoveably bent down upon the sternum. The slops with which he is attempted to be fed, with the saliva, are continually trickling from the mouth. The power of articulation is lost. The urine and faeces are passed involuntarily; and at the last, constant sleepiness, with slight delirium, and other marks of extreme exhaustion, announce the wished-for release."*

With their powers of articulation, many patients describe their condition as "tiredness" or "exhaustion". Frequently they precede the nouns with adjectives; "extreme, complete, total, or utter". Their lack of energy affects routine activities, work, leisure and social commitments. Yet the first reference to the subject, by Drs. Hoehn and Yahr, seems to be from 1967. Published papers on fatigue first appeared as recently as 1993. Not given the attention it deserves, the feeling is common and often the most troubling of all symptoms in PD.

Statistics attest to the prevalence of fatigue. Numerous studies published between 1993-2006 report the pervasiveness of fatigue in people with PD, ranging from 33% to 58%. An early study, 1993, revealed a third of PD patients consider it their single most disabling issue. Fifty-eight percent of patients rated fatigue among their 3 most

disabling symptoms and 67% reported the sentiment was qualitatively different from the fatigue they experienced prior to the onset of PD. A Dutch study also published in 1993, reported 43% of non-depressed patients felt fatigue, half developing it before the onset of illness. In the same study, 15% rated it the worst issue of PD, though 54% rated it as severe as other symptoms.

If fatigue is such an issue, why has it received so little attention? Fatigue is problematic. Not only do clinicians under-diagnose the symptom, but it is also absent from the UPDRS, the Unified Parkinson's Disease Rating Scale. Unlike tremor that is easily observed and measurable, clinicians rely on patients to communicate the problem. They use metaphors, *"It's like my energy bubble just bursts... it's like my battery runs down... my spring unwinds..."*

The Fatigue Assessment Inventory defines the symptom as, "a sense of tiredness, lack of energy or total body give out." A medical dictionary defines it as, "Weariness, usually from overexertion." Another dictionary provides synonyms, "lassitude, languor, exhaustion". The medical world has classified fatigue into subtypes. Measurable muscle fatigue is associated with overuse. The experienced subjective feeling, sometimes called central fatigue, has mental and physical features, and is defined as difficulty initiating and sustaining mental and physical tasks without physical or motor impairments. Mental fatigue is evident in shortened focus or attention, is related to both sustained hypervigilance and hypovigilance (low-level alertness), intellectual activity, emotional tension, and reduced motivation. Primary fatigue is caused by disease, secondary fatigue is caused by other problems arising from the illness, including depression.

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This newsletter explores the social, psychological, and medical picture of a puzzling disease that affects over 1.5 million Americans. It is our hope that the information contained here will be helpful and enlightening to those with Parkinson's disease, and to their families, as an expanding network of individuals maintain contact to help bring about relief and hopefully a cure.

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Fatigue is tangled with depression, sleep disruption, excessive daytime sleepiness and apathy. Until it is possible to cleanly tease one symptom from another, speaking of fatigue in those with PD is entering a world of grays, where edges of one malady blend into the next, and often depend on the words chosen. For example, patients distinguish between tiredness from strenuous exercise and the fatigue they feel. Their fatigue remains after napping, while people with sleep deficiency feel transiently refreshed. While excessive daytime sleepiness afflicts up to 50% of PD patients, studies suggest fatigue is independent and unrelated to the degree of sleepiness or nighttime sleep problems. Unlike daytime sleepiness, fatigue has no pattern. Fatigue or loss of energy experienced nearly every day is one of nine symptoms defining depressive disorder and is a potent predictor of progression to chronic depression; up to 35% of successfully treated patients with major depression continue to experience fatigue. A Norwegian study found fatigue affected nondepressed, nondemented and nonsleepy PD patients as often as those with these issues. After deep brain stimulation patients are likely to confuse apathy with fatigue, reporting tiredness and difficulty beginning activities. Patient rarely use the term "fatigue" to describe their sentiment, preferring words like "tiredness", "lack of energy" or "exhaustion". They do agree the experience is unpleasant.

Fatigue in PD contributes to a narrowing scope of life. Full-time work becomes part-time work then early retirement. One's social network narrows as professional contacts are no longer met in person, but contacted by phone, FAX or

email. Home care gradually replaces the home business. Fatigue becomes an active part in a developing feedback loop, gaining strength from pain, depression, inactivity, and deconditioning and circling, increasing one's disability.

What can be done? Treatment trials of antidepressants in those with PD are progressing. The effect such medications have on fatigue should be evident in 2-3 years. Cancer patients may use stimulants to counteract fatigue brought on by disease; stimulants may be useful in PD, also. Exercise benefits PD patients by improving function, walking ability and quality of life. Though not proven, it may aid in diminishing fatigue. The authors of the review advocate a multidisciplinary approach-employ all methods; combine drugs, exercise, physical therapy and support groups, so patients benefit by some treatment aspect, and avoid downward spiraling currents.¹

LUNGS, LEVODOPA, AND PD

The muscles of the respiratory system, slowly succumb to progression of disease in advanced PD. Disease impacts the smooth muscle surrounding each tree limb-like bronchus, the internal and external intercostal muscles running diagonally and attaching between each rib, the diaphragm, and the straight muscles of the abdomen. Not until recently has there been evidence of how early this course begins. Five Indian researchers published their results on this issue in the February 2007 edition of *Movement Disorders*.

The investigators note the prevalence of pulmonary dysfunction in early PD is uncertain. Though obstructive, restrictive and mixed types of problems are evident in the lungs of patients with advanced illness; scarce publications exist on lung function in early disease. The team undertook the research endeavor to determine if severity of lung dysfunction correlates with gender, whether any motor signs correlate with dysfunction, and to study the effect of levodopa on breathing ability.

Forty-five of the 53 subjects with PD took anti-parkinsonian medications. The average time since onset of disease was 3.3 years, and the average Hoehn and Yahr stage was 2.4, off medication. In the entire population of PD subjects, none of the women smoked nor did they have smoking histories. Nineteen men had histories of smoking; the majority frequently only consumed a few cigarettes a day for several years. None had respiratory symptoms, lung disease or known heart ailments. Investigators matched this popu-

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While it is the purpose of this newsletter to report and explain current information on Parkinson's Disease, it is not intended to furnish medical answers to individual problems. This is best done by your own doctor.

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lation with 53 control subjects of the same age and sex, for comparison.

Stage II disease has bilateral or midline involvement without impaired balance; walking ability becomes compromised. Evidence of Stage III appears with impaired righting reflexes; the patient is unsteady in turning, or has difficulty recovering balance when gently pulled backwards while in a standing position.

No PD patient had any clinical signs or symptoms of respiratory issues in the "off" state, and all reported improvement of motor symptoms with levodopa. Yet pulmonary (involving lungs) testing showed impairments in most aspects of lung function; forced vital capacity, forced expiratory volume in the first second, peak expiratory flow rate, maximum voluntary ventilation, and lastly maximum expiratory and inspiratory pressures; all were significantly lower than results from the control group. The pattern of breathing impairment indicated patients had a restrictive type of dysfunction, improving with medication, yet remaining significantly reduced when compared to the control group.

Men and women with PD were of comparable age, with the same general duration of PD. With and without medication, the Hoehn & Yahr staging scores and UPDRS scores were similar. However, women's scores on respiratory tests were consistently lower than the scores of men. While "off", 53% of women showed evidence of severe restrictive dysfunction in the lungs; decreasing to 20% while in the "on" state. When men were "off" only 10% had scores indicating severe lung disease; none had such evidence while "on". In the control population, this inequity was not apparent.

The authors conclude with the following insights. Restrictive lung disease commonly presents as dyspnoea, or shortness of breath. Reduced physical activity resulting from motor impairments might minimize the perception of the inability to catch one's breath. Though not an idea of the authors, the cultural expectations of physical activity for older upper class Indian women with illness, may lead to sedentary lifestyles with few opportunities for exertion, and less knowledge of one's respiratory impairment. Levodopa elicited significant improvement of all aspects of lung function, partially reversing dysfunction in women. The research team recommends routine measurement of inspiratory and expiratory pressures during evaluations. They note patients without motor symptoms that warrant dopaminergic medications, but suffering from shortness of breath, may find relief from respiratory ailments with these drugs.²

EARLIER SURGERY?

Neurosurgery is currently optional for those with PD who have endured the illness for 10 years or more and have motor complications limiting the quality of life. Surgeons question whether those with early PD might benefit from less restrictive conditions, making deep brain stimulation available before illness limits social function and degrades the quality of life. Yet clinicians need to eliminate any possibility a patient may be suffering from an atypical disease pattern, that would respond poorly to surgery, and time is required for aberrant symptoms to become manifest. The surgical strategy rarely is advised for patients under fifty-five years of age, but if it were an option, it might influence lives positively. A French investigative team examined this issue in a small study of twenty patients.

The investigators targeted individuals younger than 55 years of age, with a disease duration of 5 to 10 years and mild to moderate motor symptoms. Investigators split the twenty subjects into two groups. One received surgical treatment; the other underwent the "best medical treatment" defined as optimized medical treatment. All were engaged in a professional activity, had normal MRIs of the brain, and were without psychiatric disease or dementia, though illness had impaired them socially and functionally. Ten subjects underwent surgical placement of stimulators to the STN (subthalamic nucleus).

Investigators assessed all subjects 1 month prior to interventions, then at months 6, 12 and 18 months after treatment. The specific items of focus included the activities of daily living; motor examination and levodopa-induced motor complications compiled in the UPDRS (Unified Parkinson's Disease Rating Scale) parts II, III and IV. Patients reported on their disease-specific quality of life in the Parkinson Disease Questionnaire 39 and neuropsychological testing included a battery of tests evaluating possible dementia, psychiatric issues, depression and anxiety. The French team focused on the relative change in quality of life between groups and in relation to baseline testing.

Subjects receiving the "best medical treatment" experienced no significant change in their quality of life. They even worsened slightly, in the eighteen months under study. Surgical subjects improved by 24%, due to improved scores on activities of daily living, and scores of stigmatization and bodily discomfort. In assessments con-

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ducted at 6, 12 and 18 months after surgery, motor scores off medication worsened by 6%, 8% and 29% respectively, in people who underwent medical treatment. Gradual deterioration of function occurs as medications do not slow the progression of illness, they merely treat symptoms, making life more pleasant. Following surgical implantation of electrodes and off medication, but prior to the onset of stimulation, the surgical group averaged scores of slightly higher motor disability compared to those treated medically at re-assessment month 18. The authors do not comment on this data, but one may suspect the worse motor score is a result of neurosurgery and tampering in the brain. When stimulation was switched on, and without medication, improvements climbed to 59%, 64% and 69% at the respective re-assessment times. The improvements apparent in the surgical group were statistically significant from the scores of the medically treated at the three re-assessments and resulted from decreased rigidity, bradykinesia or slowness of movements, tremor and axial symptoms (relating to balance and posture).

In terms of medication, the medically treated group increased their daily doses of levodopa by an average of 9%, 17% and 12%, compared to baseline, at re-assessment months 6, 12 and 18. Motor complications induced by medications worsened by 10% and 15% after an initial improvement of 2%. In contrast, the surgical group reduced medications by 71%, 61% and 57% compared to baseline values, and motor complications fell by 76%, 83% and 83%.

"Cognition and frontal lobe function remained stable in both groups." The investigators claim mental status, in particular dementia and frontal lobe function, (for example the ability to plan, judge, discriminate, problem solve, and act spontaneously yet in a socially acceptable way) remained secure through treatments in both groups. What the authors consider stable may be an over-generalization, though no patient became truly psychotic. Psychiatric assessments showed the surgical group had significantly decreased levels of anxiety and a few subjects tended to have better moods. Four of ten individuals from this group had transient depression and five experienced episodes of mania. A patient whose PD symptoms almost completely disappeared after surgery developed a disorder in which she was unable to distinguish problems related to PD with other unexplainable motor signs. The somatoform disorder improved but persisted in the patient. Without any known medical reason,

she unexpectedly developed a new walking pattern. A more immediate issue arose in surgery; the surgical team accidentally severed the lead cable of a patient undergoing implantation of electrodes and the cable needed to be removed and replaced.

The authors state the motor improvement in the surgical group was excellent when subjects were off medication. Medication did not improve their condition beyond the performance attained when stimulation began. The authors state, "This is not surprising because the STN stimulation is expected to improve only levodopa-sensitive symptoms."... "The continuous effect of stimulation resulted in a stable and lasting best "on" condition, as shown by the attenuation of dyskinesia and motor fluctuations after surgery." The dramatic improvement in motor ability was likely the reason for the higher quality of life in the surgical group. The team found none of the subjects who underwent stimulation suffered from any cognitive deterioration or apathy, though others have reported this.

After 18 months in the study, researchers invited those who received medical treatment to undergo surgery. Eight of ten participants agreed. Surgery as early as 5 years after the onset of PD symptoms may be considered aggressive treatment. The authors would like families and patients to consider neurosurgery superior to medical treatment even in mild to moderate PD, rather than a last resort for those in advanced stages of illness. Every individual with PD must weigh the risks involved in actual surgery, the risks in healing, and the risks inherent with maintaining a working stimulator in one's brain. Once implanted, the device has an average lifespan of five years. Unfortunate events occur. Zero to 5% of patients undergoing implantation suffer from hemorrhaging, or bleeding in the brain. In younger patients, surgery may avoid medication-induced dyskinesias as well as motor fluctuations and increasing disability. Though stimulation may enhance movement, the disease progresses. How a younger population copes with deep brain stimulation, the perils of surgery, the hazards in healing, and matters of upkeep will become apparent as more people undergo early surgical treatment and studies document their health.³

PARKIN POINT MUTATIONS: HERE, THERE, EVERYWHERE

Researchers have learned approximately 50% of people with early onset PD; occurring at or before thirty years of age, harbor *parkin* muta-

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tions. Since investigators discovered the mutation's role in early-onset disease, they noted people with typical PD, late-onset, sporadic and dominant forms of the disease, also harbor the genetic quirk. Most research studies exploring the prevalence of the *parkin* mutation, found the genetic alteration rare, and absent in control subjects. This observation may lead one to suspect the presence of *parkin* is sufficient to predispose an individual to PD. Before the suspicion gains any validity, a thorough genetic investigation in control subjects will aid in determining whether the mutation truly relates to disease, or merely occurs coincidentally. A diverse group of researchers headed by Denise Kay published the findings of such an undertaking in the January 2007 edition of *Annals of Neurology*.

Their goals were threefold; analyze *parkin* sequences in PD patients and controls, determine if the mutations exist exclusively in patients, and identify novel genetic changes serving as protection against PD, present only in control subjects. The investigation occurred in two sections. Tier one enrolled 603 people from Portland, Oregon. Tier two mushroomed, involving 2,917 people from a wider geographical area. All subjects gave blood, from which the lab extracted genomic DNA for analysis.

From tier one; investigators identified 34 different *parkin* sequence variations in the 1,206 chromosomes they analyzed. Twelve of the 34 were common changes in the structure of the gene on the chromosome, while 22 were rare variants. Four of the rare variants were previously identified, while 18 were completely novel. Control subjects harbored 10 of 22 anomalies; PD patients harbored 8, and 4 mutations presented in both groups of people. There was no significant difference between patients and controls in the frequency of any mutation.

Investigators replicated the study in tier two, with a larger population. They followed two mutations of special interest, P437L and IVS8 + 48 c>t. The first mutation appeared with increased frequency in female PD patients. Past research discovered the genetic change occurs in family members affected with PD and may predispose one to the illness. However, an association was absent in the larger population study. Overall, they found no apparent difference between patients and control subjects in frequency of genetic variations, types, or locations.

The third aim of the study, assessing whether any variant of the *parkin* gene may serve as protection against PD, was impossible to determine.

A single mutation occurred more frequently in PD patients versus control subjects, but the association was lost in the larger population study. In all, investigators found no increased frequency of any variation of *parkin* amidst control subjects, so they could identify no genetic change serving to protect against PD.

We know *parkin* associated juvenile parkinsonism is an inherited genetic illness; both alleles-the spaces in the same location on a pair of chromosomes are altered. Whether a single mutation-an alteration of only one allele, or a heterozygous chromosome pair can cause, or affect the risk of contracting PD remains questionable. A study by Chien and colleagues recently provided evidence that homozygous *parkin* mutations-where identical spaces on a pair of chromosomes harbor the altered genes, cause PD. He reported on a family of 225 individuals, in which 15 had PD. All of the affected family members carried homozygous mutations and none who were heterozygous carriers were affected with disease. Other work has provided evidence supporting Chien's findings. PET (positron emission tomography) studies of people carrying heterozygous *parkin* mutations gave evidence that such individuals, though without PD symptoms, still exhibit alterations in the function of the nigral-striatal pathways, an area stricken in PD. Genetic testing for the *parkin* gene has been commercially available for several years. Future research will help dispel much of the uncertainty in our present knowledge and conclusions.⁴

TRANSDERMAL ROTIGOTINE

Yikes, another three syllable drug for PD. Do not despair. You may find this patch useful. Research suggests oral doses of levodopa contribute to motor complications by periodically stimulating dopamine receptors in the brain. Long-acting, or controlled release formulations are preferable because they minimize the periodic surges of medication occurring in blood with standard prescriptions. Another way to sustain constant dopamine levels is to take a dopamine agonist. Pramipexole and ropinirole are two non-ergotamine derived medications typically used to sustain dopamine levels. Pergolide, bromocriptine and lisuride are ergotamine-derived, or extracted from the fungus, ergot. Though many patients have no problems with the latter three medications, clinical reports have provided evidence they are capable of creating an overgrowth of tissue surrounding the heart and it's valves.

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For this reason, many clinicians prefer to recommend other types of dopamine agonists.

Before drugs are available commercially, they must be proven effective for a specific illness and safe. To establish this, the authors conducted a multicenter, double-blind study comparing a transdermal patch containing rotigotine, with a placebo or patch with no active medication. Subjects with early onset PD began treatment with a 2mg. patch. After three weeks and gradual increasing dosages, most patients were using a 6mg. patch every 24 hours. When patients experienced side effects they felt were unbearable they were advised to return to the dosage of the previous week.

To assess effectiveness of the treatment investigators compared the changes in UPDRS (Unified Parkinson Disease Rating Scale) scores and responder rates, or subjects who showed 20% improvement or more. Three hundred two subjects enrolled in the study. Investigators randomly selected 277 to undergo treatment with placebo or active medication; 96 received placebo patches, 181 received rotigotine. During the first three weeks rotigotine doses increased gradually to achieve an optimal effect for each patient, defined as the balance between the drug dosage adequate to achieve maximal reduction of symptoms without overwhelming side effects. When subjects attained this dosage, they began a 24-week maintenance phase, where they were evaluated every 4 weeks. When the maintenance phase ended, all subjects taking rotigotine got a 4-day supply of patches to begin gradual withdrawal from medication.

As patients attained therapeutic doses of rotigotine, they improved functionally as seen by decreasing scores on the UPDRS, indicating lessening of impairment. Those taking placebo also experienced improvement of PD symptoms, though not in such dramatic fashion. From the initial testing or baseline, the average decrease in PD symptoms of those applying the active drug fell by 6 points, while the average of those using placebo fell by 2.8 points. Over the maintenance phase, a 6-month period, subjects receiving rotigotine kept their improved condition, while those on placebo slid back towards baseline, and worsened by an average of 1.31 points on the UPDRS. Forty-eight percent of those using rotigotine patches experienced an average of at least 20% improvement on UPDRS scores-indicating at least a 20% reduction in impairment, while 44% averaged improvements of 25% on UPDRS scores.

Wondering about the dark side of treatment? Here it is. The authors state, adverse effects "were generally mild to moderate in intensity..." They included nausea, somnolence, dizziness and headache, symptoms common to dopamine agonists. Six percent of those in the placebo group found the side effects intolerable and withdrew from the study, while 14% in the active drug trial reported adverse affects leading to discontinuation. Other side effects that occurred less frequently were hallucinations; none of the active drug group vs. 1% of the placebo group, peripheral edema or swelling of the ankles; 3% of both groups and orthostatic hypotension or positional low blood pressure; 2% of the active drug group vs. 4% of the placebo group, experienced this negative effect.

While patch preparations of dopaminergic drugs provide distinct advantages; continuous drug delivery independent of mealtimes, sleeping hours, and the ability to swallow, problems arise under the treatment square. Forty-four percent of subjects receiving rotigotine experienced skin reactions. Wary of this possibility, investigators varied treatment locations between the abdomen, thigh, hip, flank, shoulder and upper arm. Other transdermal preparations, specifically nitroglycerine, nicotine, fentanyl, and clonidine elicit similar rates of skin reactions. The authors state, "Ninety-nine percent of the rotigotine-treated patients' application site reactions were mild to moderate in intensity, and the majority were transient in nature." Ninety-five percent of subjects who experienced the discomfort of a skin reaction completed the study, and 73% continued to use the treatment in the extension trial. While the authors feel they demonstrated the efficacy of the drug treatment, they caution the experiment was too short to determine whether patch preparations effect development of motor complications. They hope to address the longevity of treatment effect and patient health and function in the on-going extension trial, lasting three years.⁵

NET NEWS

San Jose Mercury News

Steve Johnson of the reported the National Institute of Health has decided to use the creatine formula of a tiny biotechnology company to assess whether the nutritional supplement provides benefits to those with early stage PD. Located in San Jose, California the company has only ten employees. The study will enroll 1,720 PD patients from 52 medical centers in the United

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States and Canada, and monitor subjects for up to seven years.

Belleville News Democrat

Southern Illinois University School of Medicine will be seeking volunteers for participation in the nationwide study of creatine. Those diagnosed with PD within the past five years, who are taking levodopa or similar drugs for two years or less are invited to call or contact: The National Institute of Health (800) 352-9424, or on the computer www.parkinsontrial.com.

Creatine is sold as a nutritional supplement and thought to enhance athletic ability. Research studies suggest the substance improves the function of mitochondria, which produce energy or ATP, within our cells for cellular work. Creatine may also act as an antioxidant, preventing cells from damage and degradation. In laboratory research with parkinsonian mice, creatine provides some protection against loss of dopamine-containing cells.

Malvern Gazette, UK

One hundred twenty five miles north of the Arctic Circle, a band of huskies pulled Anthony and the sledding crew through the Norwegian Lapland. Anthony Burger joined a group of determined volunteers to travel 155 miles in five days to raise money for Parkinson's disease research. His father Martin, was diagnosed fifteen years ago with the illness. Twenty-one year old Anthony discovered the organization, Across the Divide, on an internet site. He received a brochure detailing the how the charity raises money and picked the most unusual challenge. "The best part was being on the sledge, in complete silence, with just white all around you."

NeuroTalkCommunities

<http://neurotalk.psychcentral.com>

CNN-International Business News Shwetal Kamalapurkar reported from Bangalore, India: Fifty-eight-year-old Andrew Kisana was diagnosed with PD 15 years ago when he first noticed slight tremors. Gradually he lost control of his movements and his speech became slurred. Surgery was an option, though it is not always

effective for patients like Andrew. Doctors chose a newer form of treatment; bone marrow stem cell therapy. "There was about 50 per cent recovery after stem cell therapy in Andrew's condition. Earlier he had severe tremors, he could not walk, there was drooling of saliva, his speech was slurred, he could not even write. But now, after one year of therapy, he can walk. he is not having tremors, and he can write and use his computer as well," says Chief Scientific Officer, Stempeutics Research, Manipal Hospital, Dr Satish Totey. What exactly is bone marrow stem cell therapy? Stem cells from a patient's bone marrow are extracted and set aside to grow and divide. After an adequate population of stem cells has formed, they are injected back into the patient's brain, through small holes drilled in the bony cranium. Presumably, stem cells regenerate by themselves, compensating for cells lost to disease.

Capitol Games: Stem cell Speeches

<http://njmg.typepad.com/herbjackson/>

The senate passed April 10th and 11th debating over stem cells. New Jersey's Senator Frank Lautenberg's statement is an excerpt from the congressional record. "*When we look at the situation, we see that stem cells have the potential to save lives and alleviate the suffering of millions of Americans. Of course we should fully fund research for embryonic stem cells regardless of when they were developed. That is common sense. But we have a President who is held captive by ideologues who are at war with science. Over 5 years ago, President Bush enacted a policy that made no scientific sense, only political sense for his base. He put a stop to the development of new stem cell lines for research. Once again, that is a devastating blow to people who have a diabetic in their family, or cancer, Parkinson's, autism, or other diseases. We stand at a crossroads in America. We can either take the position that cells in a petri dish are a gift for healing or we can throw away the opportunity to alleviate human suffering. The men, women, and children who suffer from diabetes and other life-threatening conditions are racing against time. Recent statistics show that one out of three children born today will suffer diabetes in their lifetime.*"

PD UPDATE – THEN AND NOW

PD UPDATE has been continuously published since 1983 when it was founded by Leon C. Sack (b 1921-d 1999) of Philadelphia. Leon had suffered from PD for the last 24 years of his life. Upon learning of his diagnosis in 1979, he became dedicated to researching as much as possible about the illness. Leon came to be an expert on PD and began to publish the newsletter in order to let others know what he was able to discover about the illness and all its ramifications. Research in the field of PD and related disorders was making great strides, and he felt it was important to keep patients, family members and practitioners abreast of the latest findings. Under his guidance, the newsletter grew to be an internationally recognized source of information on PD that is mailed to approximately 10,000 doctors, pharmacists and PD patients around the world. PD UPDATE reviews recent scientific literature and translates significant articles into information that can be understood by most people. Leon was not content to just bring research findings to the average reader. He also wanted to emphasize the human face of PD by discussing issues of practical importance to patients, family and caregivers. As a consequence PD UPDATE often focused on social and psychological aspects of the illness such as caregiver stresses and the economic burden of PD, as well as discussion of new medications and surgical procedures.

Leon came to be an inspiration to others because of the remarkable way he handled his own illness for so many years. He was always encouraging to patients and family members who

would call him. He was courageous, curious and was forever searching for a better solution for himself and others.

I first met Leon and his charming wife Sylvia in 1989 when I wrote articles for the National Parkinson Foundation Quarterly Report in Miami. I was flattered to be asked by Leon to write an occasional article for his newsletter since I had been impressed with the quality and content of the copies of PD UPDATE that had crossed my desk. Over the next few years I began to write more often, and with Dr. Kathleen Clarence-Smith, we served as managing editors of the newsletter. We have been pleased to learn that many physicians, as well as patients, find the newsletter highly informative and useful. Late last year Sylvia decided to give up ownership and passed the responsibility of publisher of PDUPDATE to me. I am dedicated to continuing the outstanding tradition of reporting information on all aspects of PD to patients, caregivers and health care providers. In my effort to expand the reach of the newsletter, I am now working with the Parkinson Research Foundation, Inc., (PRF). This non-profit foundation shares with me the same dedication to the PD community. The mission of the PRF is to raise consciousness about PD, expand the educational effort and support both basic and clinical research. Together we will continue to publish the newsletter and we plan to make it available through the internet at www.parkinsonresearchfoundation.org.

~~ *Juan Sanchez-Ramos, PhD, MD,
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