

The Parkinson Alliance attended the :

The National VA Parkinson's Disease Consortium September 4 and 5, 2008, Pittsburgh, Pennsylvania

The National VA Parkinson's Disease Consortium was established in 2003 as a means to broaden the impact of the Parkinson's Disease Research, Education and Clinical Centers (PADRECCs) and encourage the delivery of modern Parkinson's disease management across the collective VA Healthcare System. While the PADRECCs serve as Centers of Excellence, the Consortium aims to revolutionize clinical care at unique VA Medical Centers through professional education, collaboration, and support.

To kick off the gathering, Dr. Robert Ruff, the National Director of Neurology, provided some background information about the PADRECCs. He indicated that the PADRECC was designed to create a network; establish a uniform approach to care; coordinate patient and caregiver education; meet the needs of an increasing population of individuals who will be diagnosed with PD; reduce the need for medical treatment outside of the VA; and ensure that the VA is in the forefront of healthcare delivery. Dr. Robert Jesse, Chief Consultant, Medical Surgical Services, followed up Dr. Ruff's introduction with emphasis about the importance of enhancing patient care at three levels: 1. Facility Level through the establishment of teaching resources – performance improvement experts; 2. Network Level – sharing knowledge across facilities; 3. National Level – creating resource centers and forums for sharing information.

The Keynote Address:

Timothy Greenamyre, M.D., Ph.D. provided an excellent keynote address. The title of his presentation was “Toward a Unified Hypothesis of Parkinson's Pathogenesis. Dr. Greenamyre discussed the complexity of Parkinson's disease (PD), particularly as it related to the multitude of symptoms that an individual with PD can experience. He proposed a different way of conceptualizing PD; specifically, he considers it a syndrome, where it is not just a constellation of the movement disorder symptoms, but the symptoms of PD include numerous non-motor symptoms that result from various changes in the brain. He discussed many of the possible causes for PD, including genetic problems, environmental factors (pesticide exposure), and unknown causes (idiopathic) of PD. A major focus of Dr. Greenamyre's presentation related to some current research that he is conducting related to Rotenone, an odorless chemical that is used as a broad-spectrum insecticide, piscicide (a chemical substance which is poisonous to fish; often used to combat parasitic and invasive species of fish), and pesticide. It occurs naturally in the roots and stems of several plants. Dr. Greenamyre has found that Rotenone mimics/causes Parkinson's disease-like symptoms, and he is conducting research regarding the mechanisms behind such a chemical, which will hopefully lead to further understanding about the process of PD and as importantly to lead to effective treatments for PD and hopefully a cure.

Debates during the Consortium:

This year's Consortium was structured such that various topics were presented and pros and cons related to each topic were debated. As such, the remainder of this summary highlights the main points from a few debates as it related to specific topics. It should be

noted that the physician's presenting on the "pros and cons" had their particular perspective "assigned" to them before the meeting and the comments below may not represent their true stance on the topic. Moreover, they were asked to merely present stimulating thoughts regarding their assigned topic to generate discussion.

Premotor PD can be diagnosed:

Matthew Stern, MD from the Philadelphia PADRECC presented the "Pro" perspective:

- Patients pre-Parkinson's disease may have more central nervous system, psychological, musculoskeletal, visual changes, sleep disturbance, and cardiovascular or other autonomic difficulties (i.e., constipation, changes in smell, orthostatic hypotension) than the general public.
- If we can identify pre-clinical symptoms of PD with a high degree of accuracy, we could conceptually intervene at an earlier period, minimizing if not stopping motor dysfunction and other debilitating symptoms.

Webster Ross, M.D. from the Honolulu Consortium presented the "Con" perspective:

- Sporadic PD would be difficult to diagnose since many of the symptoms may overlap with other medical illness.
- We could likely define "high risk" individuals for developing PD, but identifying a "pre-motor" syndrome of PD is not possible to date.
- A variety of imaging modalities (different types of x-ray machines, among other techniques) is promising, but the predictive value of these results is unknown.
- More research is needed before a clinical application is possible.

Initiation of Medication Therapy should be delayed until symptoms become disabling and bothersome.

John Duda, M.D., from the Philadelphia PADRECC presented the "Pro" perspective:

- Reducing the symptoms with medication may slow the disease progression.
- The possibility of modifying the disease progression may outweigh the medication side effects.
- The prevailing thought of delaying treatment can be harmful, as the individual with PD does better in the long run when treatment is initiated as soon as symptoms are present.

Eugene Lai, M.D. from the Houston PADRECC presented the "Con" perspective:

- By intervening early, the likelihood of optimizing quality of life for a longer period of time improves, but there are many risks to intervening early.
- Dr. Lai presented the benefits and risks of taking medications for PD, and he defined the cost-benefit ratio based on the long-term benefit versus the adverse outcome of taking the medications. For example, he stated that dopamine does not hasten the disease or lose its effectiveness with time. He noted, however, that there are many adverse side-effects, including nausea, dizziness, and dyskinesias (motor fluctuations).
- He stated that the cost/benefit ratio is "acceptable if the treatment is needed." However, he listed many medications whose cost is much greater than the benefit

- (i.e., side effects of medication may reduce quality of life and the long-term benefit of some medications is unknown).
- Thus, he concluded that initiating therapy prior to disabling symptoms may not be beneficial in the long term.

Continued dopaminergic stimulation minimizes levodopa-induced motor complications.

Jeff Bronstein, M.D. from the Southwest PADRECC presented the “Pro” perspective.

- Continuous dopaminergic stimulation minimizes Levodopa-induced motor complications.
- Motor fluctuations vary depending on age of the patient, duration of the disease, and type of therapy (e.g., medication therapy).
- The earlier the age of diagnosis and the longer one has PD results in increased motor fluctuations.
- Continuous stimulation results in decreased motor fluctuations.

Ergun Uc, M.D. from Iowa City Consortium presented the “Con” perspective:

- PD is not just a motor condition; it involves motor, cognition, psychiatric, autonomic functions, and sleep.
- Dr. Uc emphasized the importance of interpreting some research outcome with caution due to the way the research was conducted (the type of measures used; the type of statistics conducted, etc.)
- There are no robust clinical trials that have proven that continuous dopaminergic stimulation is effective.
- Some research has found that continuous dopaminergic stimulation does not minimize the motor fluctuations any more than intermittent dopaminergic stimulation.

Deep Brain Stimulation (DBS) will expand in the treatment of PD in the future.

Bill Marks, M.D. from San Francisco PADRECC presented the “Pro” perspective:

- Neuromodulation (DBS being an example) is an established approach to treatment of neurological disorders, especially movement disorders.
- In 2008, fifty thousand patients have been treated world wide.
- DBS has a rapid, robust, and persistent benefit for the appropriate patients.
- There is continual improvement in identifying the appropriate patient for DBS.
- The stimulation devices continue to improve.
- DBS is a treatment that can be tailored to specific motor symptoms.
- Some research is pointing to the neuroprotective effects of DBS.

Fred Revilla, M.D. from the Cincinnati Consortium presented on the “Con” perspective:

- DBS is indeed the most important medical development for the treatment of PD since Levodopa. However:
- It has a major limitation, in that it does not treat non-motor symptoms, and it can potentially cause some non-motor symptoms.

- PD is a complex, systemic disease (affecting multiple aspects of the human body and mind), and DBS seems to only assist in some of the symptoms (e.g., some motor symptoms, and even then, not all motor symptoms).
- There may be medical complications resulting from such an invasive procedure (although the complications are low in frequency).
- There are other treatments that we need to explore, such as gene therapy, stem cell intervention, among others.
- Dr. Revilla acknowledges that DBS is an excellent intervention, but for the sake of debate, he points out that other respectable intervention may be available and should be considered.

Dementia in PD is due to diffuse Lewy body disease.

- *Lewy bodies are abnormal “clumps” of protein that accumulate in certain structures in the brain.*
- *Dementia with Lewy Bodies is a progressive degenerative disease or syndrome of the brain that shares symptoms of both Alzheimer’s disease and Parkinson’s disease and is characterized by fluctuating cognition, hallucinations, and parkinsonism.*
- *Pathology can be defined as structural and functional changes produced by a disease process.*

Jim Leverenz, M.D. is from the Northwest PADRECC and he presented the “Pro” perspective:

- Diffuse Lewy body disease impacts the brainstem, limbic system (structures below the surface of and deep within the brain), and structures on the surface of the brain.
- Diffuse Lewy body can impair thinking skills (e.g., memory, language, attention and concentration, solving complex problems, judgment, etc.) and can cause psychiatric symptoms (e.g., hallucinations, mood disturbance, etc.).
- Diffuse Lewy body disease is the primary pathologic cause for dementia developing later in PD (as cited by other authors, such as Apaydin 2002).

John Duda, M.D. is from the Philadelphia PADRECC and he presented the “Con” perspective:

- Dementia in PD can be attributed to a few factors (such as neurocognitive difficulties attributable to PD pathology; Lewy bodies; a co-existing Alzheimer disease).
- Most studies agree that Lewy body pathology does not differ between early and late onset dementia. In other words, whether one develops dementia earlier in life versus later in life, there is not a major difference as it relates to Lewy body pathology.
- However, several studies suggest that early onset patients have more senile plaque pathology and possibly more tangle pathology than late onset (similar to patients with Alzheimer’s disease).
- The longer duration of parkinsonism before dementia related to less severe scores of amyloid plaque (a plaque consisting of tangles of amyloid protein in nervous tissue that is often considered a pathological mark of Alzheimer's disease) and α -synuclein (a protein in the brain).
- Thus, understanding Lewy body pathology is complex, and Lewy body and co-existing Alzheimer’s disease may be directly related to Parkinson’s disease dementia (PDD).

Non-motor symptoms of PD:

Daniel Weintraub, M.D. from the Philadelphia PADRECC presented some information regarding non-motor symptoms of PD.

- Depression
 - Exists in 20 to 40 percent of individuals with PD
 - Depression is higher in the elderly population in general and is probably higher in PD than in other neurodegenerative conditions or chronic diseases
 - Depression is often under-recognized in this population
 - Depression may also be mis-diagnosed due to the overlap of PD symptoms and depression symptoms (for example, sleep disturbance, appetite disturbance, fatigue, concentration/thinking changes, motor slowing).

- Anxiety
 - Exists in 40% of individuals with PD
 - Most individuals with anxiety also have depression
 - Anxiety is understudied in this population, and there is an absence of treatment studies for anxiety symptoms in this population.

- Hallucinations
 - Exists in 15 to 40% of individuals with PD.
 - There are many possible causes for hallucinations: PD medications, cognitive impairment, progression of PD.
 - Hallucinations in PD patients are prevalent for individuals with PD who have dementia.

This brief summary provides a recap of some of the highlights from the The National VA Parkinson's Disease Consortium, September 4 and 5, 2008. Should you have any questions or comments, please contact The Parkinson Alliance at 1-800-579-8440.