WHAT IS PARKINSON’S DISEASE?
Parkinson’s disease (PD) is a disorder of the central nervous system. It results from the dysfunction of a part of the brain that controls movements such as walking and balance. PD may appear at any age, but it is most common in people over the age of 50. There are cases reported in those less than 30 years old, but it is rare.

PD is a chronic and progressive condition, as it persists and its symptoms worsen over time. It is not usually inherited. However, familial forms exist and first-degree relatives of people living with PD are at slightly higher risk for the condition. Currently, there are over one million Americans living with PD.

WHAT CAUSES IT?
PD is a neurodegenerative disease. It occurs when certain nerve cells, or neurons, die or become impaired. This degeneration takes place in an area of the brain called the substantia nigra, located in the brainstem, which is one of the centers that control movement. Normally, these neurons produce a chemical known as dopamine, which is responsible for transmitting signals across the nerve pathways to produce smooth, purposeful movements. Loss of dopamine causes nerve cells to fire abnormally. This leaves people living with PD with difficulty directing or controlling their movements in a natural manner. People living with PD have usually lost 80% or more of dopamine-producing cells in the substantia nigra by the time symptoms are apparent. In addition, there is also neuronal cell loss and related pathology in other brain regions, responsible for other non-motor symptoms.

The main reason why these cells die or become impaired is still a mystery. Most scientists believe that both genetic and environmental factors are contributing causes. However, how they lead to PD is still unclear.

WHAT ARE THE SYMPTOMS?
The cardinal motor symptoms of Parkinson’s Disease are listed below:

Slowness of movement (also known as Bradykinesia): This is typically an early sign and affects almost all people living with PD. It can be disabling because it interferes with normal daily activities. Bradykinesia includes difficulties with voluntary movement planning and
execution. It is established by a decrease in speed, amplitude, dexterity and fluidity of movements. This includes decreased arm swing, changes in hand writing or micrographia, and shuffling gait. Other symptoms may include loss of facial expression, soft speech and difficulty swallowing.

**Tremor:** The tremor or involuntary shaking in PD can be seen in the hands, arms, legs, jaw or face. Typically, it starts on one side of the body, and it is visible when the affected body part is at rest or not in motion. Tremors that are present only with movement of the limb are usually due to other conditions. While it is present in many patients, approximately 25% of people living with PD never develop a tremor.

**Rigidity:** Rigidity or muscle stiffness may impair the full range of limb motion and interfere with normal activities. It may cause pain and a stooped posture.

**Postural instability:** The loss of balance reflexes known as postural instability usually begins later in the course of the disease. It can lead to falls and contributes greatly to the disability associated with PD.

PD can also cause a variety of other symptoms outside the realm of the motor system, known collectively as non-motor symptoms. The non-motor symptoms include diminished sense of smell, memory loss, sleep disturbances, depression, constipation, urinary frequency/urgency and erectile dysfunction among others.

**HOW IS PARKINSON’S DISEASE DIAGNOSED?**

Currently, there is no specific test or marker for PD. The diagnosis is made by a neurologist following an examination. An MRI of the brain may be ordered to exclude other brain diseases. However, there are no clear changes on the MRI that can conclusively tell that a person has PD.

While not everyone will develop all four cardinal symptoms, at least two are required for diagnosis, in the absence of an alternative cause (for example, exposure to certain medications or history of strokes). When symptoms first appear and signs are subtle, a precise diagnosis may be difficult.
WHAT IS THE TREATMENT?  
(treatment should be done under the guidance of a movement disorder specialist)

The treatment of PD may be challenging, but unlike other neurodegenerative diseases, there is effective symptomatic treatment. While medical and surgical therapy can provide long-lasting benefits, the goal of therapeutics in PD is neuroprotection (the development of drugs that can halt or slow down the progression). To date, no medication has demonstrated definite neuroprotection. However, monoamino oxidase inhibitors (MAO-B-) like rasagiline (Azilect®) may have disease modifying effects. There are also several other agents that have shown sufficient promise to warrant larger trials (CoQ10, creatine). In addition, the DaTSCAN was approved by the FDA and it can be used as a tool to monitor the dopamine system in Parkinson’s disease.

There are a large number of drugs available to treat the motor and non-motor aspects of PD. Symptoms can be controlled in numerous patients for many years. For most people living with PD, maintaining a healthy lifestyle, proper diet and regular daily exercise are recommended for an improved quality of life. Support groups for both patients and carepartners are beneficial for psychological support, educational information and practical advice.

DRUGS USED TO TREAT PARKINSON’S DISEASE

Levodopa: also called L-dopa, is currently the single most effective drug for the treatment of PD. It is converted into dopamine in the brain, the neurotransmitter produced by cells in the substantia nigra. Levodopa helps control the main motor symptoms of PD. It is generally taken with another drug, carbidopa, to avoid its most common side effect, nausea. In the United States, this combination is commercialized under the name carbidopa-levodopa, Sinemet®, Sinemet® CR, or StaLevo®, a single pill containing carbidopa, levodopa and entacapone. There is controversy about how early in the disease levodopa therapy should be initiated.

Dopamine agonists: are drugs that stimulate dopamine receptors directly in the brain, mimicking the effect of levodopa. These medications are used to treat the motor symptoms of PD, particularly early in the disease and in younger patients. They are not as potent as levodopa, but they delay the onset of motor complications associated with chronic levodopa use. Agonists currently available in the
United States are pramipexole (Mirapex®), ropinirole (Requip®), and apomorphine (Apokyn®). The rotigotine patch (Neupro®) was withdrawn from the U.S. market in April 2008, but it is still available in other countries.

COMT inhibitors: prevent the breakdown of dopamine in the brain. When taken with levodopa, the effect of a single dose is prolonged. The two COMT inhibitors available in United States are entacapone (Comtan®) and tolcapone (Tasmar®). A combination of levodopa, carbidopa and entacapone in a single tablet is available as StaLevo®.

Monoamineoxidase inhibitors (MAOB-I): Selegiline (Eldepryl®, Zelapar®) and rasagiline (Azilect®), the two MAOB-I commercially available for the treatment of PD, also inhibit the breakdown of dopamine in the brain, prolonging its effect. Recent trials suggest that rasagiline may have disease-modifying effects (neuroprotection). An older study on selegiline indicated that the medication also slowed down the disease. The results were however inconclusive, as the benefit could have also been explained by its symptomatic effects.

Anticholinergic medications: are drugs that block the effect of the chemical acetylcholine in the brain. Acetylcholine opposes the effect of dopamine. They are useful against tremor and stiffness. Their use is limited by their high rate of side effects. The most commonly used anticholinergic medications are trihexyphenidyl (Artane®) and benztrapine (Cogentin®). Ethpropazine (Parsitan®) is available in Canada.

Amantadine: also known as Symmetrel® can relieve the motor symptoms of PD, particularly tremor. It has a more significant effect in reducing the abnormal movements (dyskinesias) caused by chronic dopaminergic treatment.

Other agents: medications to treat depression and anxiety, constipation, urinary and erectile dysfunction, and sleep disturbances may be necessary to optimize quality of life for people living with PD.

COMPILATIONS OF DRUG TREATMENT

Most people living with PD have many years of uncomplicated treatment after the diagnosis. However, as the disease progresses over time, a significant proportion can develop treatment complications. Medication adjustments may be required to minimize them.
Motor complications of treatment:

**Motor fluctuations:** refers to as “wearing-off”, “on-off” and “dose failure”. “Wearing-off” is the shortening of the benefit period of a single medication dose. An “on-off” period is a sudden and unpredictable loss of the effect of a drug and “dose failure” is the lack of any benefit from one particular medication dose.

**Dyskinesias:** are uncontrollable, abnormal movements that may occur in people living with PD after years of treatment with Levodopa. These movements usually occur at the peak effect of a dose of Levodopa. Amantadine may ameliorate this complication, as well as deep brain stimulation.

**“Off” Dystonia:** is manifested by abnormal twisting movements, particularly of the fingers and toes. It typically occurs in the mornings before the first dose of medication.

**Freezing:** occurs when there is a sudden inability or hesitation to move (motor block). It may appear at the beginning of a movement, when going through doorways or narrow passages or when turning. It may lead to falls. Freezing does not always respond to medications.

Non-motor complications of treatment:

**Psychosis:** may result from side effects of antiparkinsonian medications. It includes hallucinations, delusions and disorientation. It may also be a feature of disease progression. Reducing and eliminating some medications can be helpful. The use of atypical antipsychotic medications, such as quetiapine (Seroquel®) or clozapine (Clozaril®), may be necessary in some cases.

**Orthostatic hypotension:** occurs when there is a drop in blood pressure upon standing. It may cause dizziness, lightheadedness and even fainting in some cases.

**BRAIN SURGERY**

When symptoms are inadequately treated with medications, brain surgery is an option. Not every person living with PD is a good candidate for surgery. An ideal candidate is an otherwise healthy person with PD who responds well to the medication but has developed severe motor complications.
There are two surgical procedures for PD: lesioning and deep brain stimulation (DBS). Lesion procedures (also known as pallidotomy or thalamotomy) deliver energy to heat and destroy a small part of the brain. These procedures are gradually being replaced by DBS, as the latter is a reversible and programmable therapy. DBS therapy uses a medical device, similar to a pacemaker, implanted in the chest wall, and a thin, flexible wire, called a lead. The lead is located deep in the brain, in three possible areas that control movement. The device sends mild electrical signals to the lead that block some of the brain messages that cause the motor symptoms. When used in an adequate candidate, DBS can lead to improvement of all motor features of PD, and many patients are able to decrease their medications. Risks of DBS include surgical risks (hemorrhage or infection) as well as hardware complications (leads breaking, electrode malfunction or battery failure). Side effects may include language impairment and walking difficulties.

**IS THERE A CURE?**

Remarkable progress has occurred in the study of PD in the last few years. To date, however, there is no known cure for the disease. For most people living with PD, symptoms can be controlled for many years, and life expectancy is not significantly reduced.

**HOW IS PARKINSON’S DISEASE RELATED TO DYSTONIA?**

Dystonia and PD are movement disorders that are closely related. First, both conditions can occur together in certain diseases. People living with PD may experience dystonia as an early symptom or as a motor complication of treatment. Dopa-Responsive Dystonia and Rapid-Onset-Dystonia-Parkinsonism are hereditary forms of dystonia in which PD is often also present. Other neurodegenerative disorders, such as Wilson’s disease, may have both dystonia and PD, in conjunction to other clinical features. Second, dystonia and PD share common treatments. Anticholinergic medications and levodopa may ameliorate both conditions, and DBS is a surgical alternative for both, although the final brain target may vary. Lastly, PD and dystonia are thought to result from dysfunction of the basal ganglia and their output, although the ultimate cause of the disorders is not known. Further research is necessary to determine the various underlying genetic, environmental, or other underlying mechanisms that may play a role in causing these two related disorders.
MAKING A DIFFERENCE

The Bachmann-Strauss Dystonia & Parkinson Foundation was established in 1995 to find better treatments and cures for the movement disorders dystonia and Parkinson’s disease, and to provide medical and patient information. Key among its efforts, the Foundation funds scientific and clinical research and helps to raise awareness of Parkinson’s disease and dystonia among the general public and the medical community.

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