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This Week's Breakthrough

The Latest Treatments for Parkinson's

In 1817, London physician James Parkinson published a paper entitled "Essay on the Shaking Palsy." Although this was the first "modern" formal description of the disease, in 175 AD the noted Greek physician Galen referred to the condition as "Shaking Palsy." Thousands of years previous, its existence was discussed in the ancient medical writings of both the Indian (Ayurveda; the disease was called "kampavata" and "atmagupta") and Chinese medical literature as long as 2,500-5,000 years ago. Parkinson's (PD) is a progressive and to date incurable neurological disorder resulting from d egeneration of dopamine-producing brain cells (neurons) in the *substantia nigra pars compacta* (SNpc) and *corpus stratia* portions of the midbrain.

When dopamine secretion from the SNpc becomes deficient, the classical symptoms of the disease begin to manifest—tremor (trembling or shaking) of a limb (often beginning in one hand), especially when the body is at rest (and less so with movement); rigidity of the limbs; poor balance; slow movement (bradykinesis) or an inability to move (akinesis); a shuffling gait; stooped posture; difficulty swallowing; difficulty speaking; and lack of facial expression ("mask face").

The most common symptom of PD is known as the "pill-rolling tremor," where there is an uncontrollable movement of the thumb resembling the rolling of a pill between the thumb and other fingers. The disease also may cause mental

disturbances including depression, personality changes, loss of sleep, and sexual problems. One tragedy of PD is that by the time any symptoms are noticed, 80-90% of the dopamine-producing cells have been lost.

> Parkinson's disease exists throughout the world with the disease being more prevalent in some countries than others, although it remains unclear why these variations occur. PD is infrequently seen in those under 40 years of age, with the average age at onset being about 60. The disease afflicts about one percent of both men and women over age 70, with men being slightly more affected than women. About 500,000 to one million people in the U.S. have PD, with roughly 50,000 additional new cases annually. (1) As the population ages, its prevalence is expected to rise. Several well-known personalities suffering from PD, including Muhammad Ali, Michael J. Fox, and the late Pope John Paul II, have brought the disease more into the public eye.

There have been many theories regarding the cause of PD—including pathogenic infection, genetic predisposition, toxic environmental exposure, and poor nutritional habits—although no single causative factor has been proven definitively, and there are likely multiple causes. The literature contains references to PD symptoms being caused by ingestion of illegal drugs contaminated with the substance MPTP. Studies of family histories and of twins suggest some may have a genetic susceptibility to PD which is influenced by environmental factors.

Whatever the ultimate causative factor(s), researchers believe there is oxidative damage to cellular structures in the SNpc area of the brain. This causes a deficiency of one of the three most important neurotransmitters, dopamine. Neurotransmitters are those chemicals that help the billions of brain cells both send and receive nerve impulses, and thereby communicate with each other.

Currently there are no blood tests or imaging techniques that can conclusively diagnose Parkinson's, although these tests are useful in excluding other diseases and identifying structural, vascular and metabolic anomalies that may be at the root of the disease. Neurologists use several means to attempt to diagnose PD, including PET and other brain scans. While not pointing to a specific diagnosis, the P300 brainwave speed and voltage test and the quantitative encephalograph (QEEG) are useful in identifying early cognitive loss.

Autopsied brains of affected victims show microscopic structures called Lewy bodies, the presence of which are considered a hallmark of classical PD. Autopsies of older persons without diagnosed PD often uncover *Lewy bodies,* a fact that has led some researchers to believe that known PD sufferers are only the tip of a much larger neuro-decaying iceberg—with as many as 20 affected people for each diagnosed PD patient. (2)

Treatment

As there is no cure for Parkinson's, therapies can only reduce its progression, minimize symptoms, and maximize the quality of life. Because PD creates a deficiency of dopamine, one form of treatment focuses on replacing dopamine with precursor substances such as levodopa (L-dopa; Sinemet® and Larodopa®), which the body converts into dopamine. One of the difficulties associated with the use of L-dopa is that it loses its effectiveness over time. Also, after about five years 50% of its users have motor complications such as

after about five years 50% of its users have motor complications such as involuntary movements (dyskinesias). (3) Additional side-effects can include nausea and vomiting, which are often treated with the addition of the drug *carbidopa*. Difficulty with swallowing, breathing and balance also can occur. (4) Despite their many potential side-effects, these drugs are often helpful in controlling Parkinson's symptoms.

Alternatively, other drugs such as selegiline (Deprenyl® and Eldepryl®) attempt to prevent the breakdown of dopamine by inhibiting *monoamine oxidase* (MAO), the enzyme that breaks down dopamine in the brain. Such drugs are referred to as MAO inhibitors. A third approach is the use of drugs such as bromocriptine (Parlodel®) and pergolide (Permax®) to directly affect dopamine receptors. Combinations of these drugs are often prescribed.

Two surgical techniques can be used in the later stages of PD, when all other forms of treatment have failed. Ablative surgery severs areas in the brain that control muscle movement, thus relieving symptoms of tremor, rigidity, and slow movement. Surgical complications can include stroke, cognitive impairment, difficulty swallowing, and vision defects. (5) Deep brain stimulation, discussed below, is another surgical procedure typically reserved for late-stage PD.

Deep Brain Stimulation

A relatively new surgical technique, Deep Brain Stimulation (DBS) is a surgical option for persons with Parkinson's disease, Essential Tremor, dystonia, and tremor resulting from multiple sclerosis. It often provides relief from tremors, rigidity, stiffness, slowness of movement, and balance problems. DBS is a new-and-improved version of the old surgical technique involving the destruction of small portions of the brain within the thalamus or globus pallidus. As currently practiced, the goal of DBS is the stimulation, not destruction, of brain tissue.

During the surgery, a small lead containing several electrodes is positioned within the brain at the specific area to be stimulated. Success of the operation depends on the correct placement of the electrodes. The target area is defined prior to the operation by use of magnetic resonance imaging (MRI), and is further defined by sophisticated monitoring instruments as well as patient-doctor interactions during the operation. Even though the patient remains awake during the surgical placement of the electrodes, the operation is painless as the brain itself does not have pain receptors and therefore does not generate pain signals. Other pain-producing tissue damage caused by the operation is treated with a local anesthetic.

The lead containing the electrodes is connected by thin, insulated wires through a small opening in the skull to an apparatus consisting of a battery and a programmable regulator (impulse generator) implanted under the skin below the collar bone in the chest area. The impulse generator, or pacemaker-like device, transmits the proper electrical signals to the target area of the brain, blocking abnormal neural activity which is the cause of the symptoms to be treated.

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On average, DBS patients experience about a 50% improvement in walking and balance, from 60-80% improvement in symptoms of tremor and slowness of movement, and over 80% reduction in involuntary movements caused by medication. Following DBS, most patients are able to significantly reduce their medication levels.

There is a 2-3% risk of brain hemorrhage that may either cause no problem, or may cause problems such as paralysis, stroke, or speech impairment. Stated another way, for each 100 patients receiving DBS, two or three will experience a severe complication or permanent damage. There is a reported 15% risk of a minor or temporary complication. DBS is an FDA-approved procedure for the treatment of Essential Tremor and Parkinson's disease, and is covered for these conditions in most states by Medicare. Most other insurance policies also cover DBS.

Stay tuned for next weeks newsletter where more natural treatments offer additional hope to those suffering from Parkinson's.

1. www.ninds.nih.gov
2. Ibid.
3. www.ivanhoe.com/channels/p_channelstory.cfm?storyid=8175
4. Tanner, C.M. Drug-induced movement disorders in Extrapyramidal Disorders. In *Handbook of Clinical Neurology,* Vol. 5. Edited by Vinken, P.J., et al. Elsevier: Amsterdam, Holland, pp. 185-204, 1986.
5. Hammerstad, J., et al. "Parkinson's disease: surgical options." *Current Neurology & Neuroscience Reports*, 1(4):313-319, July 2001.

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