

What is Parkinson's Disease?

By **Michael Rezak, MD, PhD**

Parkinson's disease (PD) is a movement disorder that is caused by the deficiency of a substance in the brain called dopamine. Dopamine is a neurotransmitter that is produced by cells (neurons) in a region of the brain known as the *substantia nigra*. When approximately 60-80% of the dopamine neurons are lost, motor symptoms of PD begin to emerge. Although we know that PD symptoms are caused by a depletion of dopamine in the brain, we do not as yet fully understand what mechanisms or conditions cause the degeneration to occur.

The diagnosis of Parkinson's disease is made on clinical grounds, meaning that the person is examined by a physician who determines whether the following cardinal features of the disease are present:

- Tremor at rest (tremor when the limb is not in use)
- Bradykinesia (slowness)
- Rigidity (stiffness)
- Loss of postural reflexes (balance problems)

Not all of these features need to be present to make the diagnosis. Currently, there is no definitive test for Parkinson's disease. Instead, there are a series of physical and cognitive assessments used by your healthcare team to determine the diagnosis and rule out the existence of other conditions that may have symptoms similar to those of PD.

It is now known that Parkinson's disease can encompass more than just motor symptoms. In some people these non-motor symptoms may affect quality of life more than the motor symptoms. They can include sleep problems, pain, loss of sense of smell, cognitive and psychiatric symptoms, and problems with blood pressure, bowel and bladder function, and sexual functioning. In a recent neuropathological study, it appears that changes in other parts of the brain may predate the loss of dopamine neurons in the substantia nigra. This could possibly explain the fact that many patients may have loss of sense of smell, sleep disorders, depression and other symptoms well before their motor symptoms begin. Currently, these changes often associated with Parkinson's disease are being further investigated in the hope of discovering ways to predict who is likely to get PD and how to prevent it.

Although the neuropathology and most clinical symptoms are the same at whatever age PD develops, there are some unique characteristics and treatment strategies that require consideration when PD occurs at an early age.

What is Young Onset Parkinson's Disease?

When Parkinson's disease is seen in individuals under the age of 40, it is called "young onset" Parkinson's disease (YOPD). However, the age range considered young onset varies somewhat depending on the source.

It is estimated that approximately 10% of the 1.5 to 2 million people with PD in the United States fall into the YOPD category, strictly defined as occurring between the ages of 21-40. The number of cases may actually be much higher than 10% of the PD population because Parkinson's disease is often overlooked as a possible diagnosis in younger patients. As a result, many young people travel a circuitous route in order to attain eventual diagnosis. Although the diagnosis is not a welcome one, for many young people it ends a lengthy process of referrals to a variety of medical specialists searching for the cause of their symptoms. Once the diagnosis is made, some express relief that this was "not just all in my head," and that they now have a name and medical treatment for what they have been experiencing.

Although both environmental and genetic causes for YOPD have been implicated, it appears genetics may play a greater role in the development of PD in those with young onset than in those with later onset. A number of genes have been identified as possible players in the development of PD, but more research is needed to determine how each of these genes specifically functions (see *Genetics* section).

Unique Characteristics of YOPD

There are some physical, emotional, and social characteristics as well as medical management implications that are unique to YOPD:

Dystonia Symptoms in up to half of those with YOPD begin with *dystonia*, an uncontrollable stiffness or cramping of a muscle group or limb. A cramp or ache in a specific area of the body, commonly in the foot or shoulder, is a very common initial symptom of young onset PD. Individuals often report “early morning dystonia” which may interrupt sleep.

Dyskinesia and Motor Fluctuation There is a greater tendency in young people to develop dyskinesias (involuntary body movements) and fluctuations in movement over time when taking the PD medication levodopa.

Disease Progression Recent data has shown that those with young onset PD tend to have a more slowly progressive course and a smoother course of the illness than their older counterparts.

Cognition (Thinking) Problems with dementia appear to occur less frequently in younger patients.

Emotional and Social Issues YOPD occurs at a time when young people already have a very full life. Managing career and family obligations along with the stress associated with the presence of a chronic disease can prove to be a challenge to all members of the family. For some, the most difficult aspect of YOPD is an uncertain future. Questions abound, such as: Will I be able to continue working? What kind of medical bills can I expect? Will I still be able to function as a nurturing parent and spouse? Fortunately, due to its typically slower progression and the considerable number of medications now available for the control of symptoms, many young people find they are able to continue the work, social, and recreational activities they enjoy for many years.

Coming to terms with the diagnosis and challenges of the disease over a lifetime can be difficult. The patient and his or her family members are likely to experience a wide range of emotions as they try to manage this unexpected change in their lives. Many find a sense of support when they are able to communicate with others who are living with YOPD. Young onset PD support groups, online discussion groups, and various programs offered by the APDA and other Parkinson's organizations offer the opportunity to meet and to share

information and resources with other young people and their families. Professional counseling can also be very beneficial. Individual counseling can provide a private place to talk about the impact PD may be having on you and your family, and family counseling can facilitate better communication between all family members and help everyone develop healthy ways of adapting.

Medical Management

Currently, no treatment has been shown to definitively slow or stop the progression of PD. Instead, therapy is directed at managing the symptoms of the disease. Treatment typically includes the use of medications and surgical intervention. Other treatment approaches include physical therapy, occupational therapy, speech therapy, and general lifestyle modifications such as diet and exercise.

Principles to be considered with regard to the medical management of Parkinson's disease are as follows:

Symptomatic Treatment Treatment usually begins when the person with YOPD feels that his or her symptoms are affecting motor or social functioning to the extent that the ability to enjoy a meaningful quality of life or maintain employment is being compromised. Treatment is typically focused on the most bothersome symptoms, and medications can often be targeted to particular symptoms, such as management of tremor.

Levodopa Currently, levodopa is considered the most effective drug for controlling the symptoms of Parkinson's disease. Levodopa is modified by brain enzymes to produce the chemical dopamine, which the brain needs to properly control muscle movement. When there is a deficiency of dopamine, it negatively affects motor functioning and results in the symptoms of PD. While almost all people with PD will be taking levodopa at some point, its use should be delayed for as long as possible, particularly in young people. This is because the length of time levodopa is taken has been shown to be related to the development of motor complications, such as excessive movements (dyskinesias) and motor fluctuations. Once introduced, levodopa should be utilized at the lowest doses possible when: 1) an inadequate response is obtained with other medications, or 2) side effects are encountered with other medications at doses required to achieve the necessary response.

Other PD Medications Because long-term use of levodopa at high dosages often leads to movement complications that can be difficult to manage, many doctors are now using a number of other medications which can be used alone or in combination with levodopa to treat PD symptoms. MAO-B inhibitors, anticholinergics, amantadine, and dopamine receptor agonists (such as Mirapex® and Requip®) may be used prior to the introduction of levodopa, and are often adequate to treat the early stages of PD for a number of years. Dopamine receptor agonists behave like dopamine but are not as potent as levodopa and are not converted into dopamine as is levodopa.

Fortunately, we are witnessing the continual development of new drug therapies for the treatment of both the motor and non-motor symptoms of PD. For the most up-to-date information on available medications, contact APDA's National Young Onset Center.

Regular Exercise A consistent exercise program, based on one's ability level, should be incorporated into the treatment regimen of each patient in order to maintain flexibility, mobility, and general well-being. Patients can develop an exercise program on their own or with a physical therapist. Many find that attending general or PD-specific exercise classes is also helpful.

Rehabilitative Therapy Adjunct therapies, such as physical therapy, can address gait and balance issues. Speech therapy (such as the Lee Silverman Voice Treatment) can be used when symptoms are troublesome or as an early intervention.

Surgical Intervention

For most people with Parkinson disease, levodopa and other medications are effective for maintaining a good quality of life. However, when medication adjustments do not continue to improve mobility or if PD medications cause significant side effects, surgical treatment may be considered. Many people with YOPD have experienced a positive response with Deep Brain Stimulation (DBS) surgery. This procedure involves inserting a thin metal lead into a targeted area of the brain. The lead contains four electrodes. A wire, attached to the lead, runs down the neck under the skin to a computerized pulse generator. This computerized device is implanted under the skin in the chest, much like a pacemaker for the heart. Electrical impulses from the electrode silence the parts of the brain that produce movement problems resulting from dopamine loss, and can decrease motor fluctuations and markedly reduce dyskinesias. DBS surgery

does not destroy brain tissue; therefore, if newer, more promising treatments develop in the future, the DBS procedure can be reversed. Although most patients still need to take medication after undergoing DBS, many find that they are able to significantly reduce the amount of medication they are taking because of the decrease in PD symptoms. The amount of symptom reduction varies from patient to patient.

The availability of DBS represents a major milestone in the treatment options for Parkinson's disease. When choosing a center for DBS surgery, look for one with an experienced DBS team. There is a learning curve in successfully implanting the DBS device, and you should seek a center that has performed the surgery many times (contact APDA's National Young Onset Center for local resources). Criteria for patient selection may vary somewhat from center to center. Although the procedure is not without some small risk, appropriate patients can gain significant improvement. Research has shown that earlier intervention provides a more robust benefit, and that activities of daily living and quality of life can be measurably improved. Furthermore, it appears that younger patients may benefit more from DBS than older patients.

As with any treatment decision, it is important to discuss the potential risks and benefits of DBS with your doctor.

Choosing Your PD Doctor

When seeking neurological care, it is best to seek a physician who has an understanding of the unique requirements of the young PD patient. This usually means a neurologist who has pursued specialized training in movement disorders. Movement disorders specialists work extensively with PD and other Parkinson's-like illnesses. Having someone who has this knowledge base as your treating physician will help you maximize symptom control while minimizing complications of treatment which ultimately translates into long-term maintenance of functional independence.