

# LEVODOPA AND ITS EFFECT AS THE DISEASE PROGRESSES

It is a well-known fact that the most effective drug for symptom control in PD is levodopa. The initial effects of levodopa are highly rewarding, and an almost complete or near complete symptom control can be achieved at low doses when treatment is started. Unfortunately, after around five years of treatment, more than 50% of individuals lose the smooth, stable, and predictable response to the drug and start experiencing fluctuations in the improvement of motor symptoms after taking levodopa, a phenomenon called motor fluctuations (Wearing OFF of the effect of medication after a few hours, delay in getting the benefit of levodopa, called delayed ON and no effect after some doses of levodopa). The individual may also experience abnormal dance -like movements affecting the neck, hands, legs and trunk after taking levodopa, which is not under their voluntary control, a phenomenon termed levodopa-induced dyskinesias. The occurrence of these complications depends on the severity of the changes in the brain , and they eventually occur in almost all patients with PD on levodopa treatment. Deep brain stimulation (DBS) is indicated as a treatment for these phenomena.

# PROGRESSION ON NON-MOTOR SYMPTOMS IN PD

Several non-motor symptoms occur in PD. Some of them, such as depression, reduced smell, sleep disorders and constipation, can even occur before the motor symptoms of PD develop. Other non-motor symptoms are bladder symptoms, anxiety, pain, sensory symptoms, sweating disturbance, loss of clarity of speech, swallowing difficulty, etc. In a recent study, it was shown that the severity of non-motor symptoms in PD progresses slowly, and there is no effect of levodopa or other medications on the rate of progression of non-motor symptoms. Cognitive decline is a major non-motor symptom in more advanced stages of PD, and up to 30% of patients may develop clinically defined dementia.



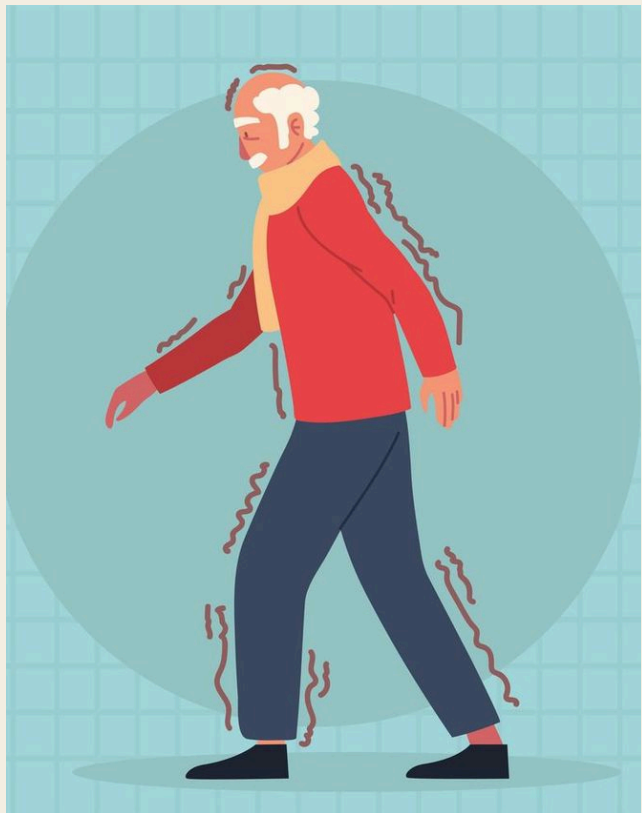
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# HOW DOES PARKINSON'S DISEASE PROGRESS?



Parkinson's Disease (PD) is a disease of the brain in which certain groups of brain cells gradually lose their ability to function and are permanently lost. It is a progressive disease, but the rate of progression is not uniform and varies from individual to individual. The factors that determine the course of the disease are not fully understood. Changes in one's genes, environmental exposure to toxic chemicals, and age at the onset of disease are some of the major determinants that influence the progression of symptoms in PD. Currently, available medications provide relief of symptoms but cannot stop the ongoing loss of brain cells in the regions affected.



## CLINICAL STAGES OF PD

Based on the evolution of diseases, PD goes through five distinct stages, which are categorized as Hoehn and Yahr stages. These stages help define the progression of the disease and the severity of movement-related symptoms (motor symptoms of PD). They do not include the non-motor symptoms of PD, which can occur at all stages and are maximum in stage V.

**Stage 1** – Very mild symptoms of PD such as tremor in the resting hand, mild slowness or stiffness confined to one side of the body. At this stage, the affected person may not experience any difficulty in performing routine tasks and may have minimal or no disability.

**Stage 2** – In this stage, symptoms are evident on both sides of the body and trunk but without impairment of balance. Quality of life is mildly impaired, and routine chores can be performed independently, though with some difficulty.

**Stage 3**—This stage indicates moderate severity of disease with mild impairment of balance. The individual can recover without any falls. There is mild to moderate disability at this stage, but the individual can still function independently.

**Stage 4**— the individual has a severe disability and may need help to do tasks but can stand or walk unassisted. The risk

of falls becomes greater, and the individual may require a walker or cane to prevent falls.

**Stage 5** – This is the stage in which patients are wheelchair-bound and require help for all activities.

The natural progression of the disease is not predictable in any individual, but those who have more walking difficulty and imbalance at onset are more likely to worsen faster than those who have predominantly tremors as the major symptoms throughout the course of the disease. Those with older age at onset of PD are more likely to develop memory and balance issues earlier.

