

# Parkinson's Disease

By

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## Overview

- Parkinson's disease (PD) is a progressive nervous system disorder that affects movement.
- Symptoms start gradually, sometimes starting with a barely noticeable tremor in just one hand.
- Parkinson's disease symptoms worsen as your condition progresses over time.

## Symptoms

- Early signs may be mild and go unnoticed.
- Symptoms often begin on one side of your body and usually remain worse on that side, even after symptoms begin to affect both sides.
- **Tremor.** Usually begins in a limb, often your hand or fingers. You may rub your thumb and forefinger back and forth, known as a pill-rolling tremor. Your hand may tremble when it's at rest.
- **Slowed movement (bradykinesia).** Over time PD may slow your movement, making simple tasks difficult and time-consuming.
- **Rigid muscles.** Muscle stiffness may occur in any part of your body.
- **Impaired posture and balance.** Your posture may become stooped, or you may have balance problems as a result of Parkinson's disease.
- **Loss of automatic movements.** You may have a decreased ability to perform unconscious movements, including blinking, smiling or swinging your arms when you walk.
- **Speech changes.** You may speak softly, quickly, slur or hesitate before talking.
- **Writing changes.** It may become hard to write, and your writing may appear small.

## Pathogenesis

- The cause of PD is unknown, but several factors appear to play a role, including:
  - **Genes.** Researchers have identified specific genetic mutations that can cause PD. But these are uncommon except in rare cases with many family members affected by PD.
  - **Environmental triggers.** Exposure to certain toxins or environmental factors may increase the risk of later PD, but the risk is relatively small.
- Researchers have also noted that many changes occur in the brains of people with PD, although it's not clear why these changes occur. These changes include:
  - **The presence of Lewy bodies.** Clumps of specific substances within brain cells are microscopic markers of Parkinson's disease. These are called Lewy bodies, and researchers believe these Lewy bodies hold an important clue to the cause of PD.
  - **Alpha-synuclein found within Lewy bodies.** Although many substances are found within Lewy bodies, scientists believe an important one is the natural and widespread protein called alpha-synuclein (a-synuclein). It's found in all Lewy bodies in a clumped form that cells can't break down.
- Risk factors for PD include:
  - **Age.** Young adults rarely experience PD. It ordinarily begins in middle or late life, and the risk increases with age. People usually develop the disease around age 60 or older.
  - **Heredity.** Having a close relative with PD increases the chances that you'll develop the disease.
  - **Sex.** Men are more likely to develop PD than are women.
  - **Exposure to toxins.** Ongoing exposure to herbicides and pesticides may slightly increase risk.

## Pathogenesis (cont.)

- PD results primarily from the death of dopaminergic neurons in the substantia nigra.
- Current PD medications treat symptoms; none halt or retard dopaminergic neuron degeneration.
- The main obstacle to developing neuroprotective therapies is a limited understanding of the key molecular events that provoke neurodegeneration. The discovery of PD genes has led to the hypothesis that misfolding of proteins and dysfunction of the ubiquitin-proteasome pathway are pivotal to PD pathogenesis.
- Previously implicated culprits in PD neurodegeneration, mitochondrial dysfunction and oxidative stress, may also act in part by causing the accumulation of misfolded proteins, in addition to producing other deleterious events in dopaminergic neurons.
- Neurotoxin-based models (particularly MPTP) have been important in elucidating the molecular cascade of cell death in dopaminergic neurons.
- PD models based on the manipulation of PD genes should prove valuable in elucidating important aspects of the disease, such as selective vulnerability of substantia nigra dopaminergic neurons to the degenerative process.

## Complications

- PD is often accompanied by these additional problems, which may be treatable:
- **Thinking difficulties.** You may experience cognitive problems (dementia) and thinking difficulties. These usually occur in the later stages of PD. Such cognitive problems aren't very responsive to medications.
- **Depression and emotional changes.** You may experience depression, sometimes in the very early stages. Receiving treatment for depression can make it easier to handle the other challenges of PD.
- **Swallowing problems.** You may develop difficulties with swallowing as your condition progresses. Saliva may accumulate in your mouth due to slowed swallowing, leading to drooling.
- **Chewing and eating problems.** Late-stage PD affects the muscles in your mouth, making chewing difficult. This can lead to choking and poor nutrition.
- **Sleep problems and sleep disorders.** People with PD often have sleep problems, including waking up frequently throughout the night, waking up early or falling asleep during the day.
- **Bladder problems.** PD may cause bladder problems, including being unable to control urine or having difficulty urinating.
- **Constipation.** Many people with PD develop constipation, mainly due to a slower digestive tract.
- **Blood pressure changes.** You may feel dizzy or lightheaded when you stand due to a sudden drop in blood pressure (orthostatic hypotension).
- **Smell dysfunction.** You may experience problems with your sense of smell. You may have difficulty identifying certain odors or the difference between odors.
- **Fatigue.** Many people lose energy and experience fatigue.
- **Pain.** Some people experience pain, either in specific areas of their bodies or throughout their bodies.
- **Sexual dysfunction.** Some people notice a decrease in sexual desire or performance.

## Diagnosis

- No specific test exists to diagnose Parkinson's disease.
- Neurologist will diagnose PD based on your medical history, a review of your signs and symptoms, and a neurological and physical examination.
- Neurologist may suggest a specific single-photon emission computerized tomography (SPECT) scan called a dopamine transporter scan (DaTscan). Although this can help support the suspicion that you have PD, it is your symptoms and neurologic examination that ultimately determine the correct diagnosis.
- Imaging tests — such as an MRI, ultrasound of the brain, and PET scans — also may be used to help rule out other disorders. Imaging tests aren't particularly helpful for diagnosing PD.

## Treatment

- PD can't be cured, but medications can help control your symptoms, often dramatically. In some more advanced cases, surgery may be advised.
- Levodopa, the most effective PD medication, is a natural chemical that passes into your brain and is converted to dopamine.
- Dopamine agonists don't change into dopamine. Instead, they mimic dopamine effects in your brain.
- MAO B inhibitors. Include selegiline, rasagiline, and safinamide. They help prevent the breakdown of brain dopamine by inhibiting enzyme monoamine oxidase B (MAO B). This enzyme metabolizes brain dopamine.
- Deep brain stimulation. Surgeons implant electrodes into a specific part of your brain. The electrodes are connected to a generator implanted in your chest near your collarbone that sends electrical pulses to your brain and may reduce your PD symptoms.

## Prevention

- Because the cause of PD is unknown, proven ways to prevent the disease also remain a mystery.
- Some research has shown that regular aerobic exercise might reduce the risk of PD.
- Some other research has shown that people who consume caffeine — which is found in coffee, tea and cola — get PD less often than those who don't drink it.
- Green tea is also related to a reduced risk of developing PD.
- However, it is still not known whether caffeine actually protects against getting PD, or is related in some other way. Currently there is not enough evidence to suggest drinking caffeinated beverages to protect against PD.

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