

Fact Sheet

Parkinson's Drug Therapy & Drug Research

What is Parkinson's Disease?

Parkinson's disease (PD) is a progressive neurological disease resulting from the destruction of nerve cells in the brain. The condition mainly affects movement, especially in the early stages. As PD progresses, various parts of the nervous system may be affected, resulting in depression, cognitive impairment and physical conditions such as bladder problems.

Different parts of the brain work together by sending signals to each other to coordinate our thoughts, movements, emotions, and senses. When we want to move, a signal is sent from the *basal ganglia* to the *thalamus* and then to the *cerebral cortex*, all different parts of the brain. Nerve cells in the brain communicate by using chemicals called neurotransmitters, which facilitate the transmission of nerve impulses between nerve cells. As we move, nerves in the basal ganglia communicate with the thalamus using a neurotransmitter called *dopamine*. When the basal ganglia cells die, they can no longer produce and send dopamine, so the signal to move doesn't get communicated. Another chemical in the brain, *acetylcholine*, is controlled by dopamine. Therefore, when the level of dopamine is too low, the level of acetylcholine becomes too high, causing the tremors and muscle stiffness that many people with PD experience.

People with Parkinson's often exhibit a "shuffling" gait, tremor of the arms and legs when they are resting (although not everyone with PD experiences tremors), muscle stiffness, and stooped posture. Some individuals

also have cognitive (thinking, judgment, memory etc.) problems.

As the disease progresses beyond minor symptoms and the person begins to have difficulty with daily activities, drug treatment may be indicated. Drug therapy for Parkinson's typically provides varying degrees of symptom relief for 10-15 years or more. The most commonly prescribed medication is *L-dopa* (levodopa) which helps replenish some of the lost dopamine in the brain. Sinemet, a combination of levodopa and carbidopa, is the drug most doctors use to treat Parkinson's disease. Your doctor may or may not begin drug treatment with Sinemet, but eventually virtually everyone diagnosed with PD is placed on Sinemet. Other drugs are also used, and new drugs are constantly being discovered and tested. It is common for multiple drugs to be prescribed, because many of them work well together to control symptoms and reduce side effects.

It is very important for people with PD to work closely with their physicians. Many of the drugs used to treat Parkinson's become less effective over time, so physicians will often try different combinations of drugs as the disease progresses. The doses of these drugs are increased or decreased for each individual, until an appropriate dose and medication schedule is achieved. Also, responses to Parkinson's drugs vary from person to person, so an individual with PD may need to work with his or her physician to find the most effective drug or combination of drugs. It may take several weeks or months before a drug begins to work. Many Parkinson's drugs can also "wear off" between doses during the day, so people with PD need to pay close attention to the

times they take their medications and plan activities carefully. In addition to discussing your medications and their dose schedules with a physician, be sure to go over them with the pharmacist when you have a prescription filled.

Any Parkinson's medications can have side effects. With some medications, the side effects are most severe when the person first begins taking the drug, then gradually disappear or lessen. With other medications, side effects may appear after weeks or even years. For example, long-term levodopa use may result in large

uncontrollable movements (nodding, twitching or jerking) called "*dyskinesias*," or "on-off" attacks where the person will become frozen (unable to move) for a few seconds or minutes. Confusion may develop as a side effect after about 8 years. Dyskinesias can also be a result of too much levodopa (Sinemet). Documenting the severity and timing of the side effects will help your doctor adjust your medications.

The following table outlines some of the drugs currently used in treatment, as well as some drugs that are under investigation:

Parkinson's Drug Therapy and Research *

Drug Type drug name (Trade Name) <i>italics</i> = experimental	Use	Possible Side Effects
<p>Dopaminergic</p> <p>Levodopa is converted in nerve cells to dopamine which helps compensate for the cells that have died.</p> <p>levodopa [also called L-dopa] levodopa/carbidopa (Sinemet)</p>	<p>Most effective drug for controlling PD symptoms. Usually combined with carbidopa (Sinemet) to increase the amount getting to the brain and to reduce side effects. Works well for slowness (bradykinesia) and rigidity; only slightly improves tremors and may not help balance and other motor symptoms. Becomes less effective over time, so dose is often increased over time. Does not work for 25% of people with PD.</p>	<p>Uncontrolled movements (dyskinesias), unpredictable "on-off" responses, nausea, vomiting, low blood pressure, dizziness, restlessness, mental changes, sleepiness, visual hallucinations, confusion, personality changes, realistic dreams, and freezing episodes ("on-off").</p>
<p>Dopamine Agonists</p> <p>These drugs act like dopamine in that they send the same message to nerve cells. They are less likely to result in dyskinesias, because dyskinesias are actually caused by too much dopamine. Researchers believe they may have a neuroprotective effect.</p> <p>bromocriptine (Parlodel) [usually given with L-dopa] pramipexole (Mirapex) ropinirole (Requip) pergolide (Permax)</p>	<p>Some physicians recommend using dopamine agonists before levodopa therapy because they can improve tremors, rigidity and slow movements and have relatively few side effects. But side effects such as confusion or hallucinations appear to be more common in the over-65 age group.</p> <p>These are not effective in treating postural problems, freezing or dementia.</p> <p>When used in combination with levodopa, people require less levodopa and experience fewer "wearing off" or "on-off" problems.</p> <p>People who don't respond to levodopa often don't respond to dopamine agonists.</p>	<p>Nausea, vomiting, loss of appetite, malaise, low blood pressure, skin discoloration, visual hallucinations, confusion.</p> <p>May make levodopa-induced dyskinesias worse.</p> <p>Suddenly falling asleep — which may be a hazard.</p> <p>Scar-like tissue formation in lining of lungs, gut and abdominal tissue (rare).</p> <p>Side effects differ depending on the drug.</p> <p>May also result in unwanted drug interactions when used in combination with other medications.</p>

*This list may not be complete: new drugs are being discovered and tested all the time. Ask your physician about new treatments and clinical trials.

Drug Type drug name (Trade Name) <i>italics</i> = experimental	Use	Possible Side Effects
<p>COMT Inhibitors</p> <p>These drugs lengthen the time that levodopa remains in the brain, which makes it more effective.</p> <p>entacapone (Comtan)</p> <p>tolcapone (Tasmar)</p> <p>Use is extremely limited due to liver toxicity.</p>	<p>Used in conjunction with carbidopa/levodopa, these lower the amount of levodopa required (usually resulting in a reduction in dose) and help with “wearing off” and “on-off” problems.</p> <p>Better tolerated than bromocriptine (Parlodel).</p> <p>Improves balance and motor functions and can help with fatigue caused by dyskinesias.</p>	<p>May increase risk of dyskinesias. Nausea, diarrhea, posture problems, difficulty sleeping, vivid dreams.</p> <p>Sometimes changes the color of urine to reddish-orange or brown, which is not harmful.</p> <p>Thus far, liver toxicity has not been reported with entacapone. May also result in unwanted drug interactions.</p>
<p>MAO Inhibitors (selective for MAO-B)</p> <p>Help the dopamine in the brain last longer.</p> <p>Neither vitamin E nor selegiline appear to have a neuroprotective affect in PD.</p> <p>selegiline (Eldepryl)</p> <p>Selegiline may be used alone or in combination with levodopa; however, the combination is not as potent as the COMT inhibitor/levodopa used together.</p>	<p>Sometimes used as the first drug treatment, but becomes less effective over time.</p> <p>When used in combination with levodopa, individuals can take less levodopa and may have fewer difficulties between doses.</p>	<p>Some physicians think this drug is harmful when used over a long period of time; however, recent evidence suggests people taking selegiline and levodopa live as long as those taking only levodopa.</p> <p>The precise role for selegiline in the treatment of PD remains to be determined.</p> <p>May have serious side effects when used with some antidepressants.</p>
<p><i>rasagiline</i></p>	<p>Experimental studies indicate it rescues dying neurons.</p> <p>Currently under investigation.</p>	

Drug Type drug name (Trade Name) <i>italics</i> = experimental	Use	Possible Side Effects
Antiexcitatory May help prevent nerve cells in the brain from dying. <i>remacemide</i>	In experiments with animals, helps levodopa work better. Currently under investigation.	
Trophic Factors May protect nerve cells from damage and help damaged cells repair themselves. <i>GDNF (glial cell line-derived neurotrophic factor)</i>	Seems to reduce the side effects of levodopa and help control symptoms. Currently under investigation.	
Immunomodulators (includes anti-inflammatory drugs) Experiments indicate that these drugs may help damaged nerve cells regrow. <i>GPI-1046</i>	Currently under investigation.	
<i>cabergoline</i>	Not currently approved for use in treating PD in the US.	Has the advantage of once daily dosing.
Anti-viral Increases the amount of dopamine released by brain cells and has anticholinergic properties, and may have anti-glutamine activity, as well. amantadine (Symmetrel)	May decrease dyskinesia in some late-stage PD. May be used alone or in combination. Sometimes used in early stages. Effect wears off after a few weeks. May be effective again after stopping use for awhile. Appears to be prescribed less frequently than in past years.	Leg swelling, purple blotching of the legs, confusion, hallucinations, depression, nightmares, blurred vision. Note: doses must be adjusted downward in individuals with reduced kidney function.

Drug Type drug name (Trade Name) <i>italics</i> = experimental	Use	Possible Side Effects
<p>Anticholinergics</p> <p>These drugs block acetylcholine, which can cause tremors and muscle stiffness when too much is present.</p> <p>trihexyphenidyl (Artane)</p> <p>benztropine (Cogentin)</p> <p>procyclidine (Kemadrin)</p> <p>biperiden (Akineton)</p>	<p>Most helpful for tremor and stiffness and less helpful for slowness, balance, and walking problems.</p> <p>May also help with excess sweating and drooling.</p> <p>May be started before levodopa and/or given in conjunction with levodopa.</p> <p>Rarely prescribed for elders, especially those 75 or older. Older adults are more sensitive to the side effects caused by these drugs.</p> <p>Only work for 50% of people with PD.</p>	<p>Dry mouth, dry eyes, blurred vision, constipation, memory problems, confusion, hallucinations, difficulty urinating, increased heart rate.</p> <p>Can worsen the effects of narrow angle glaucoma.</p>
<p>Atypical antipsychotic</p>	<p>Used to control hallucinations, paranoia, or other symptoms of psychosis.</p>	<p>This class of drugs can cause extrapyramidal symptoms (uncontrollable jerky movements) and pseudoparkinsonian signs and symptoms, such as tremors or tardive dyskinesia. It is therefore very important for individuals with PD to work closely with their physicians and pharmacists to minimize side effects.</p> <p>Other side effects include orthostatic hypotension (low blood pressure upon standing), sleepiness, seizures and headache.</p>
<p>risperidone (Risperdal)</p>	<p>Used to control hallucinations, paranoia, or other symptoms of psychosis.</p>	<p>Risperdal may decrease the effectiveness of levodopa (Sinemet).</p> <p>Requires close monitoring in individuals with kidney or liver problems.</p> <p>May also result in sexual dysfunction, gastrointestinal problems, agitation and insomnia.</p>

Drug Type drug name (Trade Name) <i>italics</i> = experimental	Use	Possible Side Effects
Atypical Antipsychotics (cont'd)		
olanzapine (Zypexa)	Used to control hallucinations, paranoia, or other symptoms of psychosis.	Other potential side effects of olanzapine include agitation, insomnia, dry mouth and gastrointestinal problems.
quetiapine fumarate (Seroquel)	Used to control hallucinations, paranoia, or other symptoms of psychosis.	Other potential side effects of Seroquel include abdominal pain, agitation, and constipation.
clozapine (Clorazil)	Used to control hallucinations, paranoia, or other symptoms of psychosis.	Clorazil can result in a reduction of white blood cells, so weekly blood tests must be done. Other potential side effects of Clorazil include hypersalivation and constipation.

The information on side effects contained here is not exhaustive. Any changes in health, behavior, or feelings should be reported to your physician. Do not stop taking your medication or change the dosage unless you have discussed it with your physician.

Web Resources for Medication Information

The Internet can be a great source of information but always discuss the information you find with your physician and pharmacist to be sure that it is accurate and applicable to your situation.

IQ Health

www.subscribex.com/iqhealth/searchdrug.html

AgeNet

www.agenet.com

MedicineNet

www.medicinenet.com

The Merck Manual Home Edition

www.merckhomeedition.com

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Family Caregiver Alliance (FCA) seeks to improve the quality of life for caregivers through education, services, research and advocacy.

Through its National Center on Caregiving, FCA offers information on current social, public policy and caregiving issues and provides assistance in the development of public and private programs for caregivers.

For residents of the greater San Francisco Bay Area, FCA provides direct family support services for caregivers of those with Alzheimer's disease, stroke, head injury, Parkinson's and other debilitating brain disorders that strike adults.

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