Parkinson's Disease

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Purpose

This course explains the pathophysiology, staging, clinical manifestations, and treatment options (including their adverse effects) of Parkinson's disease.

Goal

Upon completion of this course, the healthcare provider should be able to:

- Define Parkinson's disease.
- Discuss the pathophysiology of Parkinson's disease, including the role of dopamine.
- List 6 forms of parkinsonism.
- Describe two different staging systems.
- List and describe the 4 cardinal manifestations of Parkinson's disease.
- Describe at least 8 additional common symptoms.
- Describe the primary medications used to treat Parkinson's disease.
- Describe 4 common adverse effects related to anti-Parkinson medications.
- Describe 2 surgical options involving ablation of brain tissue.
- Discuss deep brain stimulation (DBS).

Introduction

Parkinson's disease (also referred to as simply Parkinson disease) is a progressive neurological movement disorder of the basal ganglia caused by loss of dopamine-producing cells. It is characterized by bradykinesia (slow movement), rigidity,

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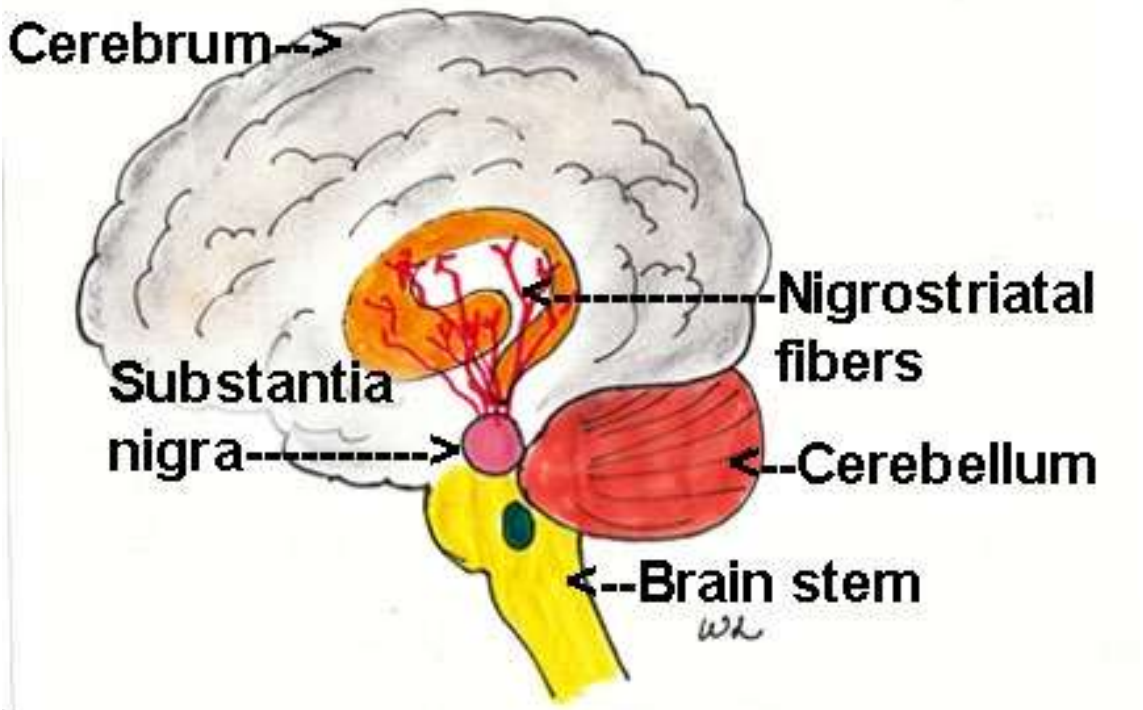
resting tremor, and postural instability with loss of postural reflexes, and a stooped, slow shuffling gait.

The incidence of Parkinson's disease increases with age, with a peak in the 50s, although an early-onset form of the disease strikes much earlier, as does drug-induced Parkinsonism. There is no definitive diagnostic procedure for Parkinson's disease, so the diagnosis is made on the basis of clinical manifestations.

Parkinson's disease is the 4th most common neurological disease, affecting 1% of those over 65 and 2% of those over 85. Approximately 1 million people in the United States have Parkinson's disease with about 60,000 new cases diagnosed each year. Incidence in men is 1.5 times the incidence in women.

Pathophysiology



Dopamine (DA), a neurotransmitter, is the critical element in Parkinson's disease, which results in progressive degeneration of the pigmented dopamine-producing neurons in the substantia nigra of the midbrain, disrupting the average balance between DA and acetylcholine (ACh) in the basal ganglia area of the brain.

The basal ganglia are a large group of nuclei at the base of the cerebral cortex. The basal ganglia control movement and coordination and affect voluntary movement. The basal ganglia interact with other essential brain structures, such as the cerebral cortex.

In a normal brain, dopamine is produced from levodopa (L-DOPA), which is itself produced from tyrosine, through interaction with the enzyme, tyrosine hydroxylase. Other enzymes also interact with L-DOPA and with dopamine.

Neurotransmitters are either excitatory (such as ACh) or inhibitory (such as DA), and in a normal brain the balance of neurotransmitters controls complex body movements. Nigrostriatal fibers project from the substantia nigra to the corpus striatum, carrying messages to the higher motor centers in the cerebral cortex. The loss of dopamine stores results in more excitatory neurotransmitters than inhibitory transmitters. This imbalance affects voluntary movement.

Symptoms usually become evident when 60% of pigmented neurons are lost and dopamine levels fall about 80%. The extrapyramidal tracts that control semiautomatic function and coordination of movements are impaired although motor cells are not damaged. The damage to the extrapyramidal tracts results in tremors, rigidity, bradykinesia, and postural instability, the key symptoms of Parkinson's disease.

Parkinson's disease is the most common form of parkinsonism, a syndrome characterized by similar symptoms but with various etiologies.

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Forms of parkinsonism	
Idiopathic	This form has no known cause and has onset usually in the 50s or 60s. This includes most cases of Parkinson's disease.
Toxin-associated	Carbon monoxide, manganese (from exposure in copper mines), carbon disulfide.
Medication-associated	Reserpine, methyldopa, lithium, haloperidol, and phenothiazine, metoclopramide have all been implicated. Symptoms may be reversible if the medications are discontinued.
Illicit-drug-associated	Methyl-4-phenyl-1,2,5,6-tetrahydropyridine (MPTP), amphetamine, methamphetamine may cause parkinsonism. MPTP is a neurotoxin that selectively destroys dopaminergic neurons in the

	substantia nigra.
Early-onset PD (<40)	Early-onset PD is believed related to genetic defects and affects about 10% of those with Parkinson's disease. Symptoms are similar to idiopathic Parkinson's disease.
Juvenile-onset PD (<20)	This rare form is usually inherited as an autosomal recessive genetic disorder although some cases are idiopathic. Symptoms are similar to adult onset Parkinson's disease. Juvenile-onset PD is usually a slowly progressive disorder, but the course varies among individuals.

Staging of Parkinson's disease

A number of different staging systems are used to describe Parkinson's disease. A staging system developed by Hoehn and Yahr has been used for many years and often guides initial treatment.

Hoehn & Yahr stages of Parkinson's disease	
I (Early stage)	• Signs and symptoms on only one side of the body • Symptoms mild. • Symptoms inconvenient but not disabling • Tremors usually in one limb • Changes in posture, locomotion, and facial expression noticeable to family and friends.
II	• Symptoms on both sides of the body. • Minimal disability. • Posture and gait affected.
III (Moderate)	• Significant slowing of body movements • Early impairment of equilibrium when walking or standing. • Moderately severe generalized dysfunction.
IV (Advanced)	• Severe symptoms • The person still able to walk to a limited extent • Rigidity and bradykinesia present • Person no longer able to live alone. • Tremor less than earlier stages.
V	• Cachectic stage (general reduction in vitality and strength of body and mind) • Invalidism complete • Person unable to stand or walk • Requires constant nursing care.

Medications, such as MAO inhibitor, anticholinergic, and/or a dopamine agonist, are usually started in stage I or stage II, but levodopa/carbidopa are usually started in stage III.

The Unified Parkinson Disease Rating Scale

The UPDRS **[SEE APPENDIX A]** is a much more comprehensive tool that requires interview, physical examination, assessment, and observation. Most items in the tool are scored from 0 to 4 with higher numbers indicating increased disability or impairment. Topics covered in the scale include:

- Mentation, behavior, and mood.
- Activities for daily living during "on" and "off" periods.
- Motor examination.
- Complications of therapy during the previous week.
- Modified Hoehn and Yahr staging.
- Schwab and England Activities of Daily Living Scale.

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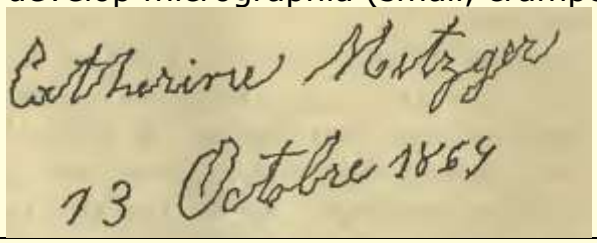
Clinical manifestations

Parkinson's disease has a gradual onset and slow progression of symptoms, which usually begin with a mild tremor in one limb and progress to both sides and severe impairments of most body functions. The 4 cardinal signs include tremor, rigidity, bradykinesia, and postural instability.

Cardinal manifestations of Parkinson's disease	
Tremor	Often the first symptom, tremor is more noticeable at rest and may involve "pill rolling" movement of forefinger and thumb or pronation-supination (slow turning) of the forearm. About 75% of patients have unilateral resting tremor on diagnosis. Tremors may involve the diaphragm, tongue, lips, and jaw, but tremor of the head rarely occurs. Tremor is noticeable when the patient is at rest and tends to increase with walking, concentration, and feelings of anxiety. Tremor may be noticeable with handwriting. Some develop micrographia (small, cramped handwriting). 
Rigidity	Rigidity is characterized by resistance to passive limb

	movements. Cogwheeling (passive exercise resulting in jerky incremental movement) often occurs. When one limb is engaged in voluntary active movement, the other limb is often stiff. Stiffness of the limbs, face, and posture are typical and may cause shoulder pain early in the disease. Because rigidity inhibits the alternating contraction and relaxation of muscles, movement is often slow and jerky.
Bradykinesia	Physical and chemical alterations in the basal ganglia and other structures in the central nervous system result in loss of automatic movements, such as blinking the eyes, swinging the arms, swallowing saliva, changing facial expressions, and making minor postural adjustments. Because of this, the patient moves slowly and may have difficulty initiating movement, such as standing from a sitting position. This also accounts for the stooped posture, drooling, masked facies (deadpan expression), and shuffling gait (festination) that are typically seen in PD.
Postural instability	As PD progresses, the patient develops characteristic postural and gait problems, usually standing with the head bent forward and walking with a propulsive gait, often walking with increasing speed and shuffling gait as the patient tries to move the feet under the body's center of gravity to maintain balance. Patients are at increased risk of falls because of difficulty pivoting. The pull test is used to evaluate postural instability. While the patient is standing, the examiner gives a moderately forceful backwards tug and observes how the patient recovers. The normal response is to step backward to prevent a fall. The examiner must be ready to catch the person with postural instability.

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In addition to the cardinal manifestations, patients may exhibit a wide range of other symptoms. Every individual is unique, so Parkinson's disease may manifest in different ways. For example, while tremors are very common, some people do not have tremors but have postural instability or other problems.

Other symptoms associated with Parkinson's disease	
Freezing	Freezing or hypokinesia is characterized by abnormally diminished ability to move so that the patient feels "frozen" to the ground for a period of time.

Dementia	Forty to 70% of patients with PD eventually develop some degree of dementia, including cognitive, perceptual, and mental deficits. Symptoms are similar to Alzheimer's disease. Some exhibit psychiatric manifestations, including psychosis, personality changes, and pronounced confusion, especially those who are elderly.
Dysphagia/ Drooling	As the muscles in the tongue, mouth, and throat are impaired, spontaneous swallowing is delayed. Sitting in upright position while eating and eating a semisolid diet with thick liquids may help promote swallowing. Teaching the patient to focus on the steps to swallowing can help. Additionally, the typical flexed neck position causes saliva to accumulate in the front of the mouth so that drooling occurs. Exercises to improve muscle coordination may provide some relief. Some patients suck on sour candies to trigger swallowing.
Depression	Mild to moderate depression occurs in 60% of those with Parkinson's disease possibly because the disease causes chemical changes in the brain. Counseling, exercise, and antidepressants may help alleviate depression.
Sleep disturbance	Tremors and stiffness often interfere with sleep. Some people also have vivid nightmares or hallucinations and may act out violent dreams. Over time, patients may sleep more in the daytime and develop sleep-awake reversal patterns. Some have relief by taking extra anti-Parkinson's medication or sleeping medication at bedtime. People should avoid caffeine or other stimulants in the evening.
Dysphonia	Weakness and incoordination of muscles result in soft, slurred, low pitched voice that is less audible.
Constipation	Constipation results from a combination of weak muscles, medication, inadequate diet, and lack of exercise. Rigidity and slow activity of the pelvic floor muscles may impair the ability to bear down to defecate. Increasing fluid and fiber in the diet, regular exercise, and stool softeners may reduce constipation.
Cramping	When medications begin to wear off, such as during the night, some people may experience dystonia—painfully forced or twisted postures that result in foot and leg cramps. Usually cramping disappears with the

	next dose of medication.
Dysuria	Urinary frequency and urgency are common and may be related to prostate disease in males. Bladder training, medications, modifications in fluid intake, and protective pads may be indicated.
Sexual impairment	Erectile dysfunction and vaginal dryness are common problems as well as loss of libido although some people experience hyperactive sexual drives related to levodopa and dopamine agonists.

Treatment options

The goal of Parkinson's treatment is to relieve symptoms and maintain function. As yet, no drugs have been able to substantially alter the progress of the disease. The primary treatments aim to correct an imbalance of neurotransmitters in the central nervous system.

Medications

Medications enhance the release or supply of dopamine (DA) or antagonize (block) the effects of overactive cholinergic neurons in the striatum. Levodopa (DA precursor), the primary drug, is central to treatment, but only a small portion of the drug actually makes it to the brain and converts to DA because much of each dose is absorbed by the body or converted to dopamine outside of the brain. Other medications are added to enhance the effect of levodopa and allow more to cross into the brain.

Medications	
Levodopa	**Action:** This primary medication is a precursor to DA and able to cross the blood-brain barrier. Levodopa is converted to DA in the basal ganglia by dopa decarboxylase (enzyme), relieving symptoms. However, levodopa may cause oxidation that may, in fact, damage the substantia nigra and speed progression of the disease, so treatment is often delayed when symptoms are mild. Additionally, levodopa has many negative adverse effects, such as dyskinesia, not found with anticholinergics (commonly used early in the disease). Levodopa is most effective in the first few years of treatment. **Adverse effects:** Prolonged use results in decreased benefit and confusion, hallucinations,

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	depression, and sleep alterations. Dyskinesia (involuntary movements, grimacing, jerking, head bobbing, chewing movements, smacking movement) may occur within 5 to 10 years of use.
Carbidopa	**Action:** Carbidopa is usually given in combination with levodopa (Sinemet®) because it inhibits dopa decarboxylase in peripheral tissues. This enzyme breaks down levodopa before it reaches the brain, so carbidopa slows the breakdown of levodopa and allows more to reach the brain, so lower doses of levodopa can be given. The effectiveness of carbidopa tends to wane in a few years so some physicians delay use of carbidopa, and begin therapy with levodopa and a dopamine receptor agonist instead. **Adverse effects:** Confusion, constipation, diarrhea, dizziness, drowsiness, dry mouth, headache, loss of appetite, nausea, taste changes, trouble sleeping, upset stomach, urinary tract infection, vomiting.
Sinemet®	This is a combination drug with both carbidopa and levodopa in fixed ratios of 1:4 and 1:10. Treatment is often started with a 1:4 mixture of 25mg carbidopa to 100 mg levodopa. Sinemet CR is a controlled release formula that is also available in various strengths.
Dopamine (DA) receptor agonists	DA agonists, such as bromocriptine (Parlodel®), pramipexole (Mirapex®), ropinirole (Requip®), and rotigotine (Neupro®), directly stimulate DA receptors and mimic the effects of DA. DA agonists may be used early in treatment rather than levodopa and carbidopa when symptoms are mild or added to the regimen of medications when levodopa and carbidopa lose effectiveness. Two newer DA agonists, ropinirole and pramipexole are often used as first-line treatment in early stages of PD. **Adverse effects:** Nausea, vomiting, diarrhea, hypotension, lightheadedness, impotence, and psychiatric abnormalities.
Anticholinergics	**Action:** Anticholinergics, such as benztropine mesylate (Cogentin®), biperiden (Akineton®), cycrimine (Pagitane®), and trihexyphenidyl (Artane®), inhibit the neurotransmitter

	acetylcholine to counteract decreased dopamine activity. Anticholinergics are used in conjunction with levodopa to reduce tremors. **Adverse effects:** Blurred vision, flushing, rash, constipation, urinary retention, and acute confusion. May be poorly tolerated in the elderly, and intraocular pressure must be monitored. Contraindicated in those with narrow-angle glaucoma. Patients with prostatic hypertrophy must be monitored for urinary retention.
Antiviral agent (Amantadine hydrochloride)	**Action:** Amantadine hydrochloride (Symmetrel®) may release dopamine from neuronal storage (action not clear). Symmetrel® helps to decrease levodopa-induced dyskinesia, rigidity, tremor, and bradykinesia, and postural changes primarily during the early stages of Parkinson's. The drug is usually only effective for a few months. **Adverse effects:** (Low incidence) Mood changes, confusion, depression and hallucinations, peripheral edema, nausea, epigastric distress, urinary retention, headache, and visual impairment.
Monamine oxidase (MAO) inhibitor (Selegiline®)	**Action:** Selegiline (Eldepryl®, Carbex®, Anipyrl®, Atapryl®, Zelapar®) inhibits breakdown of dopamine, increasing levels in the brin, and may slow disease progression. Selegiline is sometimes used with a dopamine agonist early in the disease to delay use of levodopa/carbidopa. Selegiline may also be taken with levodopa/carbidopa to decrease dose of these drugs, decreasing the "wearing off" of the drugs, and extending the period during which levodopa/carbidopa will control symptoms of PD. **Adverse effects:** Dizziness, fainting, dry mouth, nausea, vomiting, stomach pain, dysphagia, heartburn, diarrhea, constipation, sleep disorders, drowsiness, depression, muscle pain, and rash. Contraindicated with tricyclic antidepressants.
Catechol-O-methyl transferase (COMT) inhibitors	**Action:** Entacapone (Comtan®) and tolcapone (Tasmar®) increase the duration of action of levodopa/carbidopa with given in combination with those drugs because COMT inhibitors block an enzyme that metabolizes levodopa, allowing more

	to be converted into DA in the brain. COMT inhibitors also reduce motor fluctuations in advanced disease. COMT inhibitors may be taken during periods when levodopa "wears off" and is having little effect. Because COMT inhibitors allow more levodopa to enter the brain, side effects of levodopa may increase, required a decreased dosage of levodopa. **Adverse effects:** Diarrhea (most common), dark yellow/orange-discolored urine, headache, and abdominal pain. **NOTE:** Tolcapone has been linked to liver failure, so it is used only if other treatment options have failed, and the patient must have frequent monitoring of liver function tests.
Tricyclic antidepressants	**Action:** Tricycle antidepressants, such as amitriptyline, are used to treat depression associated with PD, but doses are usually only a half to a third the normal dose. Amitriptyline is the most commonly prescribed because of its anticholinergic effects. SSRIs, which also effectively treat depression, tend to increase symptoms of PD so are usually avoided. **Adverse effects:** Dry mouth, blurred vision, cardiac abnormalities, constipation, urinary retention, and hyperthermia, cognitive impairment, drowsiness, anxiety, muscle twitching, breast enlargement, and suicidal ideation may occur. Tricyclic antidepressants are contraindicated with MAO inhibitors and cimetidine.
Acetyl-cholinesterase inhibitors	**Action:** Alzheimer's drug, such as such as rivastigmine (Exelon®), donepezil (Aricept®), and galantamine (Reminyl®) may be used to treat Parkinson-associated dementia, but response is often mild and short acting. The only currently FDA approved drug for PD is Exelon®. **Adverse effects:** Nausea, diarrhea, insomnia, headache, vomiting, dizziness, fatigue, muscle aches, and depression.
Antihistamines	**Action:** Antihistamines, such as diphenhydramine hydrochloride (Benadryl®), orphenadrine citrate (Banflex®) and phenindamine hydrochloride (neo-Synephrine®) produce mild anticholinergic and sedative effects and may reduce tremors.

	Adverse effects: Constipation, diarrhea, dizziness, drowsiness, excitability, headache, loss of appetite, nausea, nervousness or anxiety, difficulty sleeping, upset stomach, vomiting; weakness.
Atypical antipsychotics	**Action:** Olanzapine (Zyprexa®), quetiapine (Seroquel®), risperidone (Risperdal), or clozapine (Clozaril®) may be used to reduce confusion and psychotic symptoms that may be iatrogenic. Clozapine is most effective but must be closely monitored. **Adverse effects:** Clozapine may cause bone marrow suppression. Side effects vary depending on the drug but may include hyperglycemia, diabetes, weight gain, impaired sexual performance, and insulin resistance.

It would be ideal if one medication regimen was adequate for all patients with Parkinson's disease, but this simply isn't the case. Patients, for example, may need to choose between rigidity and dyskinesia (a common side effect of medications). Schedules of medication may become quite complicated with a variety of different drugs taken at different times to facilitate different types of activities. Antiparkinson drugs are associated with a number of distinctive adverse effects.

For reasons that are not clear, patients often experience **"on" and "off" periods,** often during the same day. That is, during the "on" period, the medications are working and the patient is able to function. During the "off" period, the medications seem to have little effect. These wearing-off symptoms usually appear after about 5 years. Some patients can break the "off" period by taking extra medications. Patients often divide their day according to "on" and "off periods. Sometimes stopping medications for a few days and then restarting them will "reset" the medications so they work again. The process of controlling Parkinson's disease with medications can be frustrating and stressful for patients

Dopaminergic medications result in **dyskinesias**, involuntary twisting and writhing motions. Many people associate these movements with Parkinson's disease, but they are not part of the disease but rather an

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adverse effect of medications used to treat the disease. Dyskinesias usually develop within about 5 to 10 years of treatment.

Visual hallucination are also a common side effect of medications and occur most frequently when visibility is poor such as in the evening or during the night. Patients may imagine they see animals, people, or faces. Some hallucinations are frightening and related to paranoid thoughts. Many people are able to recognize that they are having hallucinations, but some persist in thinking the hallucinations are real.

Because dopamine plays an important role in experiencing pleasure, some people taking anti-Parkinson medications develop **addictive behaviors**, such as compulsive shopping, gambling, and engaging in compulsive sexual behaviors or watching pornography. Others may exhibit excessive eating, Internet use, or substance abuse. Reducing or changing medications may reduce these behaviors.

Thalamotomy and pallidotomy

These surgical procedures are done with the head immobilized in a stereotactic frame. The surgeon makes a burr hole through the skull and passes an electrode to the target area and uses electrical stimulation to ablate tissue. The purpose of these procedures is to interrupt the nerve pathways in order to alleviate tremors and rigidity. These procedures are reserved for those with idiopathic Parkinson's disease no longer responding to medications. Bilateral procedures have considerably higher morbidity than when surgery is confined to one side.

- **Thalamotomy** involves destruction of part of the ventrolateral portion of the thalamus in order to reduce tremor. Complications include ataxia and hemiparesis.

- **Pallidotomy** involves destruction of part of the ventral aspect of the medial globus pallidus in order to reduce rigidity, bradykinesia, and dyskinesia. Complications include hemiparesis, stroke, cognitive impairment, speech difficulties, dysphagia, and changes in vision.

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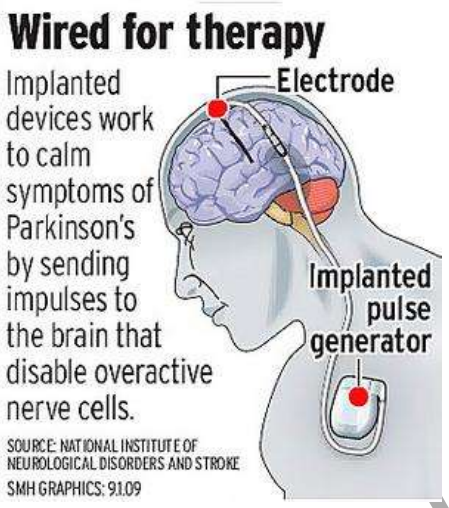
Because of the morbidity associated with these procedures, they have been largely supplanted by deep brain stimulation, which is reversible and does not require ablation of brain tissue.

Deep brain stimulation

Deep brain stimulation (DBS) involves pacemaker-like brain implants to relieve symptoms, such as tremors. Stimulation can be unilateral or bilateral, but bilateral stimulation of the subthalamic nucleus seems more effective than other surgical procedures.



Electrodes are placed in the thalamus and connected to a pulse generator implanted in a subclavicular or abdominal pouch. The pulse generator is battery powered and sends high frequency electrical impulses through wires placed under the skin to the leads anchored to the skull.

A randomized study of 255 patients with Parkinson's disease compared the best medical therapy (BMT) with DBS and found that DBS provided the most improvement in symptoms with patients receiving DBS having an average of 4.6 increased "on" hours each day, a significant improvement. Patients experienced increased confusion during the first 3 months of the study, but this abated in the last 3 months, and those with DBS reported significant improvements in quality of life.

Despite the potential for improvement, DBS is a surgical procedure that carries risk of brain damage, hemorrhage, and death. Those receiving DBS had 3.8 times more adverse effects than those on BMT. Adverse effects included gait disturbances, falls, motor dysfunction, balance impairment, depression, dystonia (with involuntary movements), and dyskinesias. Falls resulted in other injuries, including fractures, dislocations, and head trauma.

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Physical/Occupational therapy

While physical and occupational therapy don't alter the course of the disease, they can help the patient maintain good muscle tone, increase range of motion, flexibility and strength and teach techniques to help improve movement and prevent falls. Patients are taught to use adaptive equipment and to modify activities. Patients may learn strategies to combat symptoms of the disease, such as dysphagia.

Exercises/Activities may include:

- Walking, riding a stationary bicycle, and swimming maintain joint mobility.
- Postural exercises help keep the head erect.
- Stretching improves range of motion and flexibility.
- Warm baths and massage relax muscles and relieve muscle spasms.
- Special walking techniques offset the shuffling gait and tendency to lean forward while walking. Techniques include arm swinging, use of wide gait, focusing on the horizon, and a heel-toe placement with long strides.
- Walking with a metronome or music may provide sensory reinforcement.
- Combining walking and breathing exercises helps to aerate lungs and use muscles necessary for breathing.

The occupational therapist evaluates the need for environmental modifications and adaptive devices to assist the patient in self-care activities as well as employment activities.

Speech therapy

Despite speech problems associated with Parkinson's disease, only 3 to 4% of patients work with a speech therapist. Speech approaches that focus on articulation and rate of speech have shown little success. However, a new approach that was funded by a NIDCD grant shows promise.

The Lee Silverman Voice Treatment (LSVT) focuses on simple tasks to improve voice and respiratory function. The program helps patients increase loudness of speech by increasing effort and includes sensory awareness training. Patients exhibit more stable motor speech output, better ability to convey emotions from facial expressions, and improved swallowing (in some patients).

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Conclusion

A number of clinical trials are taking place in an attempt to find a drug that is neuroprotective. As yet, no cure for the disease is in sight, but researchers hope to delay progress of the disease. Research continues to explore the transplantation of porcine neuronal cells and human fetal and stem cells, although research has been stymied by restrictions on the use of fetal cells.

Gene therapy holds promise for future treatment. Gene products can be delivered directly to the affected areas of the brain by using viruses (such as adenovirus and lentivirus) for transport. Animal studies show that gene therapy can prevent death of the neurons and halt or reverse symptoms associated with Parkinson's disease.

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APPENDIX A

UNIFIED PARKINSON'S DISEASE RATING SCALE (UPDRS)
This rating tool follows the course of Parkinson's disease over time. Some sections require multiple grades assigned to each extremity. A total of 199 points is possible with 0 = no disability and 199 = total disability.

I. MENTATION, BEHAVIOR AND MOOD

1. Intellectual Impairment

0 = None.
1 = Mild. Consistent forgetfulness with partial recollection of events and no other difficulties. 2 = Moderate memory loss, with disorientation and moderate difficulty handling complex problems. Mild but definite impairment of function at home with need of occasional prompting.
3 = Severe memory loss with disorientation for time and often to place. Severe impairment in handling problems.
4 = Severe memory loss with orientation preserved to person only. Unable to make judgments or solve problems. Requires much help with personal care. Cannot be left alone at all.

2. Thought Disorder (Due to dementia or drug intoxication)

0 = None.
1 = Vivid dreaming.
2 = "Benign" hallucinations with insight retained.
3 = Occasional to frequent hallucinations or delusions; without insight; could interfere with daily activities.
4 = Persistent hallucinations, delusions, or florid psychosis. Not able to care for self.

3. Depression

0 = None.
1 = Periods of sadness or guilt greater than normal, never sustained for days or weeks.
2 = Sustained depression (1 week or more).
3 = Sustained depression with vegetative symptoms (insomnia, anorexia, weight loss, loss of interest).
4 = Sustained depression with vegetative symptoms and suicidal thoughts or intent.

4. Motivation/Initiative

0 = Normal.

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1 = Less assertive than usual; more passive.
2 = Loss of initiative or disinterest in elective (non-routine) activities.
3 = Loss of initiative or disinterest in day-to-day (routine) activities.
4 = Withdrawn, complete loss of motivation.

II. ACTIVITIES OF DAILY LIVING *(for both "on" and "off")*

5. Speech

0 = Normal.
1 = Mildly affected. No difficulty being understood.
2 = Moderately affected. Sometimes asked to repeat statements.
3 = Severely affected. Frequently asked to repeat statements.
4 = Unintelligible most of the time.

6. Salivation

0 = Normal.
1 = Slight but definite excess of saliva in mouth; may have nighttime drooling.
2 = Moderately excessive saliva; may have minimal drooling.
3 = Marked excess of saliva with some drooling.
4 = Marked drooling, requires constant tissue or handkerchief.

7. Swallowing

0 = Normal.
1 = Rare choking.
2 = Occasional choking.
3 = Requires soft food.
4 = Requires NG tube or gastrotomy feeding.

8. Handwriting

0 = Normal.
1 = Slightly slow or small.
2 = Moderately slow or small; all words are legible.
3 = Severely affected; not all words are legible.
4 = The majority of words are not legible.

9. Cutting food and handling utensils

0 = Normal.
1 = Somewhat slow and clumsy, but no help needed.
2 = Can cut most foods, although clumsy and slow; some help needed.
3 = Food must be cut by someone, but can still feed slowly.
4 = Needs to be fed.

10. Dressing

0 = Normal.
1 = Somewhat slow, but no help needed.
2 = Occasional assistance with buttoning, getting arms in sleeves.
3 = Considerable help required, but can do some things alone.
4 = Helpless.

11. Hygiene

0 = Normal.
1 = Somewhat slow, but no help needed.
2 = Needs help to shower or bathe; or very slow in hygienic care.
3 = Requires assistance for washing, brushing teeth, combing hair, going to bathroom.
4 = Foley catheter or other mechanical aids.

12. Turning in bed and adjusting bed clothes

0 = Normal.
1 = Somewhat slow and clumsy, but no help needed.
2 = Can turn alone or adjust sheets, but with great difficulty.

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3 = Can initiate, but not turn or adjust sheets alone.
4 = Helpless.

13. Falling (unrelated to freezing)
0 = None.
1 = Rare falling.
2 = Occasionally falls, less than once per day.
3 = Falls an average of once daily.
4 = Falls more than once daily.

14. Freezing when walking
0 = None.
1 = Rare freezing when walking; may have start hesitation.
2 = Occasional freezing when walking.
3 = Frequent freezing. Occasionally falls from freezing.
4 = Frequent falls from freezing.

15. Walking
0 = Normal.
1 = Mild difficulty. May not swing arms or may tend to drag leg.
2 = Moderate difficulty, but requires little or no assistance.
3 = Severe disturbance of walking, requiring assistance.
4 = Cannot walk at all, even with assistance.

16. Tremor (Symptomatic complaint of tremor in any part of body.)
0 = Absent.
1 = Slight and infrequently present.
2 = Moderate; bothersome to patient.
3 = Severe; interferes with many activities.
4 = Marked; interferes with most activities.

17. Sensory complaints related to parkinsonism
0 = None.
1 = Occasionally has numbness, tingling, or mild aching.
2 = Frequently has numbness, tingling, or aching; not distressing.
3 = Frequent painful sensations.
4 = Excruciating pain.

III. MOTOR EXAMINATION

18. Speech
0 = Normal.
1 = Slight loss of expression, diction and/or volume.
2 = Monotone, slurred but understandable; moderately impaired.
3 = Marked impairment, difficult to understand.
4 = Unintelligible.

19. Facial Expression
0 = Normal.
1 = Minimal hypomimia, could be normal "Poker Face".
2 = Slight but definitely abnormal diminution of facial expression.
3 = Moderate hypomimia; lips parted some of the time.
4 = Masked or fixed facies with severe or complete loss of facial expression; lips parted 1/4 inch or more.

20. Tremor at rest (head, upper and lower extremities)
0 = Absent.
1 = Slight and infrequently present.
2 = Mild in amplitude and persistent. Or moderate in amplitude, but only intermittently present.
3 = Moderate in amplitude and present most of the time.

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4 = Marked in amplitude and present most of the time.

21. Action or Postural Tremor of hands

0 = Absent.
1 = Slight; present with action.
2 = Moderate in amplitude, present with action.
3 = Moderate in amplitude with posture holding as well as action.
4 = Marked in amplitude; interferes with feeding.

22. Rigidity (Judged on passive movement of major joints with patient relaxed in sitting position. Cogwheeling to be ignored.)

0 = Absent.
1 = Slight or detectable only when activated by mirror or other movements.
2 = Mild to moderate.
3 = Marked, but full range of motion easily achieved.
4 = Severe, range of motion achieved with difficulty.

23. Finger Taps (Patient taps thumb with index finger in rapid succession.)

0 = Normal.
1 = Mild slowing and/or reduction in amplitude.
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
4 = Can barely perform the task.

24. Hand Movements (Patient opens and closes hands in rapid succession.)

0 = Normal.
1 = Mild slowing and/or reduction in amplitude.
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
4 = Can barely perform the task.

25. Rapid Alternating Movements of Hands (Pronation-supination movements of hands, vertically and horizontally, with as large an amplitude as possible, both hands simultaneously.)

0 = Normal.
1 = Mild slowing and/or reduction in amplitude.
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
4 = Can barely perform the task.

26. Leg Agility (Patient taps heel on the ground in rapid succession picking up entire leg. Amplitude should be at least 3 inches.)

0 = Normal.
1 = Mild slowing and/or reduction in amplitude.
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
4 = Can barely perform the task.

27. Arising from Chair

(Patient attempts to rise from a straightbacked chair, with arms folded across chest.)

0 = Normal.
1 = Slow; or may need more than one attempt.

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2 = Pushes self up from arms of seat.
3 = Tends to fall back and may have to try more than one time, but can get up without help. 4 = Unable to arise without help.

28. Posture

0 = Normal erect.
1 = Not quite erect, slightly stooped posture; could be normal for older person.
2 = Moderately stooped posture, definitely abnormal; can be slightly leaning to one side.
3 = Severely stooped posture with kyphosis; can be moderately leaning to one side.
4 = Marked flexion with extreme abnormality of posture.

29. Gait

0 = Normal.
1 = Walks slowly, may shuffle with short steps, but no festination (hastening steps) or propulsion.
2 = Walks with difficulty, but requires little or no assistance; may have some festination, short steps, or propulsion.
3 = Severe disturbance of gait, requiring assistance.
4 = Cannot walk at all, even with assistance.

30. Postural Stability (Response to sudden, strong posterior displacement produced by pull on shoulders while patient erect with eyes open and feet slightly apart. Patient is prepared.)

0 = Normal.
1 = Retropulsion, but recovers unaided.
2 = Absence of postural response; would fall if not caught by examiner.
3 = Very unstable, tends to lose balance spontaneously.
4 = Unable to stand without assistance.

31. Body Bradykinesia and Hypokinesia (Combining slowness, hesitancy, decreased armswing, small amplitude, and poverty of movement in general.)

0 = None.
1 = Minimal slowness, giving movement a deliberate character; could be normal for some persons. Possibly reduced amplitude.
2 = Mild degree of slowness and poverty of movement which is definitely abnormal. Alternatively, some reduced amplitude.
3 = Moderate slowness, poverty or small amplitude of movement.
4 = Marked slowness, poverty or small amplitude of movement.

IV. COMPLICATIONS OF THERAPY *(In the past week)*

A. DYSKINESIAS

32. Duration: What proportion of the waking day are dyskinesias present? (Historical information.)

0 = None
1 = 1-25% of day.
2 = 26-50% of day.
3 = 51-75% of day.
4 = 76-100% of day.

33. Disability: How disabling are the dyskinesias? (Historical information; may be modified by office examination.)

0 = Not disabling.
1 = Mildly disabling.
2 = Moderately disabling.
3 = Severely disabling.
4 = Completely disabled.

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34. Painful Dyskinesias: How painful are the dyskinesias?

0 = No painful dyskinesias.
1 = Slight.
2 = Moderate.
3 = Severe.
4 = Marked.

35. Presence of Early Morning Dystonia (Historical information.)

0 = No
1 = Yes

B. CLINICAL FLUCTUATIONS

36. Are "off" periods predictable?

0 = No
1 = Yes

37. Are "off" periods unpredictable?

0 = No
1 = Yes

38. Do "off" periods come on suddenly, within a few seconds?

0 = No
1 = Yes

39. What proportion of the waking day is the patient "off" on average?

0 = None 1 = 1-25% of day.
2 = 26-50% of day.
3 = 51-75% of day.
4 = 76-100% of day.

C. OTHER COMPLICATIONS

40. Does the patient have anorexia, nausea, or vomiting?

0 = No
1 = Yes

41. Any sleep disturbances, such as insomnia or hypersomnolence?

0 = No
1 = Yes

42. Does the patient have symptomatic orthostasis?

(Record the patient's blood pressure, height and weight on the scoring form)
0 = No
1 = Yes

V. MODIFIED HOEHN AND YAHR STAGING

STAGE 0 = No signs of disease.
STAGE 1 = Unilateral disease.
STAGE 1.5 = Unilateral plus axial involvement.
STAGE 2 = Bilateral disease without impairment of balance.
STAGE 2.5 = Mild bilateral disease with recovery on pull test.
STAGE 3 = Mild to moderate bilateral disease; some postural instability; physically independent.
STAGE 4 = Severe disability; still able to walk or stand unassisted.
STAGE 5 = Wheelchair bound or bedridden unless aided.

VI. SCHWAB AND ENGLAND ACTIVITIES OF DAILY LIVING SCALE

100% = Completely independent. Able to do all chores without slowness, difficulty or impairment. Essentially normal. Unaware of any difficulty.
90% = Completely independent. Able to do all chores with some degree of slowness, difficulty and impairment. Might take twice as long. Beginning to be aware of difficulty.

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80% = Completely independent in most chores. Takes twice as long. Conscious of difficulty and slowness.
70% = Not completely independent. More difficulty with some chores. Three to four times as long in some. Must spend a large part of the day with chores.
60% = Some dependency. Can do most chores, but exceedingly slowly and with much effort. Errors; some impossible.
50% = More dependent. Help with half, shower, etc. Difficulty with everything.
40% = Very dependent. Can assist with all chores, but few alone.
30% = With effort, now and then does a few chores alone or begins alone. Much help needed.
20% = Nothing alone. Can be a slight help with some chores.
10% = Severe invalid. Totally dependent, helpless. Complete invalid.
0% = Vegetative functions such as swallowing, bladder and bowel functions are not functioning. Bedridden.

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