Parkinson disease

Parkinson disease is a progressive disorder of the nervous system. The disorder affects several regions of the brain, especially an area called the substantia nigra that controls balance and movement.

Often the first symptom of Parkinson disease is trembling or shaking (tremor) of a limb, especially when the body is at rest. Typically, the tremor begins on one side of the body, usually in one hand. Tremors can also affect the arms, legs, feet, and face. Other characteristic symptoms of Parkinson disease include rigidity or stiffness of the limbs and torso, slow movement (bradykinesia) or an inability to move (akinesia), and impaired balance and coordination (postural instability). These symptoms worsen slowly over time.

Parkinson disease can also affect emotions and thinking ability (cognition). Some affected individuals develop psychiatric conditions such as depression and visual hallucinations. People with Parkinson disease also have an increased risk of developing dementia, which is a decline in intellectual functions including judgment and memory.

Generally, Parkinson disease that begins after age 50 is called late-onset disease. The condition is described as early-onset disease if signs and symptoms begin before age 50. Early-onset cases that begin before age 20 are sometimes referred to as juvenile-onset Parkinson disease.

Frequency

Parkinson disease affects more than 1 million people in North America and more than 4 million people worldwide. In the United States, Parkinson disease occurs in approximately 13 per 100,000 people, and about 60,000 new cases are identified each year.

The late-onset form is the most common type of Parkinson disease, and the risk of developing this condition increases with age. Because more people are living longer, the number of people with this disease is expected to increase in coming decades.

Causes

Most cases of Parkinson disease probably result from a complex interaction of environmental and genetic factors. These cases are classified as sporadic and occur in people with no apparent history of the disorder in their family. The cause of these sporadic cases remains unclear.

Approximately 15 percent of people with Parkinson disease have a family history of this disorder. Familial cases of Parkinson disease can be caused by mutations in the \textit{LRRK2}, \textit{PARK7}, \textit{PINK1}, \textit{PRKN}, or \textit{SNCA} gene, or by alterations in genes that have not
been identified. Mutations in some of these genes may also play a role in cases that appear to be sporadic (not inherited).

Alterations in certain genes, including GBA and UCHL1, do not cause Parkinson disease but appear to modify the risk of developing the condition in some families. Variations in other genes that have not been identified probably also contribute to Parkinson disease risk.

It is not fully understood how genetic changes cause Parkinson disease or influence the risk of developing the disorder. Many Parkinson disease symptoms occur when nerve cells (neurons) in the substantia nigra die or become impaired. Normally, these cells produce a chemical messenger called dopamine, which transmits signals within the brain to produce smooth physical movements. When these dopamine-producing neurons are damaged or die, communication between the brain and muscles weakens. Eventually, the brain becomes unable to control muscle movement.

Some gene mutations appear to disturb the cell machinery that breaks down (degrades) unwanted proteins in dopamine-producing neurons. As a result, undegraded proteins accumulate, leading to the impairment or death of these cells. Other mutations may affect the function of mitochondria, the energy-producing structures within cells. As a byproduct of energy production, mitochondria make unstable molecules called free radicals that can damage cells. Cells normally counteract the effects of free radicals before they cause damage, but mutations can disrupt this process. As a result, free radicals may accumulate and impair or kill dopamine-producing neurons.

In most cases of Parkinson disease, protein deposits called Lewy bodies appear in dead or dying dopamine-producing neurons. (When Lewy bodies are not present, the condition is sometimes referred to as parkinsonism.) It is unclear whether Lewy bodies play a role in killing nerve cells or if they are part of the cells' response to the disease.

**Inheritance Pattern**

Most cases of Parkinson disease occur in people with no apparent family history of the disorder. These sporadic cases may not be inherited, or they may have an inheritance pattern that is unknown.

Among familial cases of Parkinson disease, the inheritance pattern differs depending on the gene that is altered. If the LRRK2 or SNCA gene is involved, the disorder is inherited in an autosomal dominant pattern, which means one copy of an altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with the condition.

If the PARK7, PINK1, or PRKN gene is involved, Parkinson disease is inherited in an autosomal recessive pattern. This type of inheritance means that two copies of the gene in each cell are altered. Most often, the parents of an individual with autosomal recessive Parkinson disease each carry one copy of the altered gene but do not show signs and symptoms of the disorder.
When genetic alterations modify the risk of developing Parkinson disease, the inheritance pattern is usually unknown.

Other Names for This Condition
- Parkinson’s disease
- PD
- primary parkinsonism

Diagnosis & Management

Genetic Testing Information
- What is genetic testing?
- Genetic Testing Registry: Parkinson disease 1
- Genetic Testing Registry: Parkinson disease 3
- Genetic Testing Registry: Parkinson disease 4
- Genetic Testing Registry: Parkinson disease 5
- Genetic Testing Registry: Parkinson disease 6, autosomal recessive early-onset
- Genetic Testing Registry: Parkinson disease 7
- Genetic Testing Registry: Parkinson disease 8, autosomal dominant
- Genetic Testing Registry: Parkinson disease 10
- Genetic Testing Registry: Parkinson disease 11
- Genetic Testing Registry: Parkinson disease 12
- Genetic Testing Registry: Parkinson disease 13
• Genetic Testing Registry: Parkinson disease 14

• Genetic Testing Registry: Parkinson disease 15

• Genetic Testing Registry: Parkinson disease 16

• Genetic Testing Registry: Parkinson disease 17

• Genetic Testing Registry: Parkinson disease 18

• Genetic Testing Registry: Parkinson disease, late-onset

• Genetic Testing Registry: Parkinson disease, mitochondrial

Research Studies from ClinicalTrials.gov
• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22parkinson+disease%22

Other Diagnosis and Management Resources
• GeneReview: Parkinson Disease Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1223

• GeneReview: VPS35-Related Parkinson Disease
  https://www.ncbi.nlm.nih.gov/books/NBK447258

• MedlinePlus Encyclopedia: Parkinson's Disease
  https://medlineplus.gov/ency/article/000755.htm

• Michael J. Fox Foundation for Parkinson's Research: What Drugs Are Used to Treat Parkinson's Disease and How Do They Work?

• National Institute of Neurological Disorders and Stroke: Deep Brain Stimulation for Parkinson's Disease
  https://www.ninds.nih.gov/Disorders/All-Disorders/Deep-Brain-Stimulation-Parkinsons-Disease-Information-Page

• Parkinson's Disease Foundation: Diagnosis
  https://www.parkinson.org/understanding-parkinsons/diagnosis

• Parkinson's Disease Foundation: Treatment
  https://www.parkinson.org/understanding-parkinsons/treatment
Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Parkinson's Disease
  https://medlineplus.gov/ency/article/000755.htm
- Encyclopedia: Parkinson's Disease - Resources
  https://medlineplus.gov/ency/article/002196.htm
- Health Topic: Lewy Body Disease
  https://medlineplus.gov/lewybodydisease.html
- Health Topic: Parkinson's Disease
  https://medlineplus.gov/parkinsonsdisease.html

Genetic and Rare Diseases Information Center

- Parkinson disease
  https://rarediseases.info.nih.gov/diseases/10251/parkinson-disease

Additional NIH Resources

- National Human Genome Research Institute: Learning About Parkinson's Disease
- National Institute of Environmental Health Sciences: Parkinson's Disease
  https://www.niehs.nih.gov/health/topics/conditions/parkinson/index.cfm
- National Institute of Environmental Health Sciences: Parkinson's Disease and Environmental Factors
  https://www.niehs.nih.gov/health/assets/docs_p_z/the_role_of_the_environment_in_parkinsons_disease_508.pdf
- National Institute of Neurological Disorders and Stroke: Challenges, Progress, and Promise
  https://www.ninds.nih.gov/Disorders/All-Disorders/Parkinsons-Disease-Information-Page
- National Institute of Neurological Disorders and Stroke: Deep Brain Stimulation for Parkinson's Disease
  https://www.ninds.nih.gov/Disorders/All-Disorders/Deep-Brain-Stimulation-Parkinsons-Disease-Information-Page
- National Institute of Neurological Disorders and Stroke: Focus On Parkinson's Disease Research
  https://www.ninds.nih.gov/Current-Research/Focus-Disorders/Parkinsons-Disease
- National Institute of Neurological Disorders and Stroke: Hope Through Research
• National Institute of Neurological Disorders and Stroke: Information Page  
https://www.ninds.nih.gov/Disorders/All-Disorders/Parkinsons-disease-Information-Page

• National Institute of Neurological Disorders and Stroke: Life and Death of a Neuron  
https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Life-and-Death-Neuron

• National Institute on Aging  
https://www.nia.nih.gov/health/parkinsons-disease

Educational Resources

• Centre for Genetics Education (Australia)  

• MalaCards: early-onset parkinson's disease  
https://www.malacards.org/card/early_onset_parkinsons_disease

• MalaCards: parkinson disease, late-onset  
https://www.malacards.org/card/parkinson_disease_late_onset

• Nemours Foundation: Kids Health  

• Orphanet: Hereditary late-onset Parkinson disease  
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=411602

• Orphanet: NON RARE IN EUROPE: Parkinson disease  
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=319705

• Orphanet: Young-onset Parkinson disease  
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2828

Patient Support and Advocacy Resources

• American Parkinson Disease Association  
https://www.apdaparkinson.org/

• Bachmann-Strauss Dystonia and Parkinson Foundation  
http://www.dystonia-parkinson.org/

• Michael J. Fox Foundation for Parkinson's Research  
https://www.michaeljfox.org/

• Parkinson's Disease Foundation  
https://www.parkinson.org/understanding-parkinsons/what-is-parkinsons

• Parkinson's Resource Organization  
http://www.parkinsonsresource.org/
• The Parkinson Alliance
  https://www.parkinsonalliance.org/
• The Parkinson's Institute
  http://www.theipi.org/

Clinical Information from GeneReviews
• LRRK2-Related Parkinson Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1208
• Parkin Type of Early-Onset Parkinson Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1478
• Parkinson Disease Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1223
• PINK1 Type of Young-Onset Parkinson Disease
  https://www.ncbi.nlm.nih.gov/books/NBK26472
• VPS35-Related Parkinson Disease
  https://www.ncbi.nlm.nih.gov/books/NBK447258

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Parkinson+Disease%5BMAJR%5D%29+AND+%28Parkinson+disease%5BTIAB%5D%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• PARKINSON DISEASE 1, AUTOSOMAL DOMINANT
  http://omim.org/entry/168601
• PARKINSON DISEASE 2, AUTOSOMAL RECESSIVE JUVENILE
  http://omim.org/entry/600116
• PARKINSON DISEASE 3, AUTOSOMAL DOMINANT
  http://omim.org/entry/602404
• PARKINSON DISEASE 4, AUTOSOMAL DOMINANT
  http://omim.org/entry/605543
• PARKINSON DISEASE 5, AUTOSOMAL DOMINANT, SUSCEPTIBILITY TO
  http://omim.org/entry/613643
• PARKINSON DISEASE 6, AUTOSOMAL RECESSIVE EARLY-ONSET
  http://omim.org/entry/605909
• PARKINSON DISEASE 7, AUTOSOMAL RECESSIVE EARLY-ONSET
  http://omim.org/entry/606324
• PARKINSON DISEASE 8, AUTOSOMAL DOMINANT
  http://omim.org/entry/607060
• PARKINSON DISEASE 10
  http://omim.org/entry/606852
• PARKINSON DISEASE 11, AUTOSOMAL DOMINANT, SUSCEPTIBILITY TO
  http://omim.org/entry/607688
• PARKINSON DISEASE 12
  http://omim.org/entry/300557
• PARKINSON DISEASE 13, AUTOSOMAL DOMINANT, SUSCEPTIBILITY TO
  http://omim.org/entry/610297
• PARKINSON DISEASE 14, AUTOSOMAL RECESSIVE
  http://omim.org/entry/612953
• PARKINSON DISEASE 15, AUTOSOMAL RECESSIVE EARLY-ONSET
  http://omim.org/entry/260300
• PARKINSON DISEASE 16
  http://omim.org/entry/613164
• PARKINSON DISEASE 17
  http://omim.org/entry/614203
• PARKINSON DISEASE 18, AUTOSOMAL DOMINANT, SUSCEPTIBILITY TO
  http://omim.org/entry/614251
• PARKINSON DISEASE, LATE-ONSET
  http://omim.org/entry/168600
• PARKINSON DISEASE, MITOCHONDRIAL
  http://omim.org/entry/556500

Medical Genetics Database from MedGen
• Parkinson disease

Sources for This Summary
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16495942
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20421364
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2875048/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22013209
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16543934

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16003110

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17068789

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15297154

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16171459

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19735092

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16131423

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16026116

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20506312  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3056147/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15717024  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC534935/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15172778

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19846850  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2856322/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15955578

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17385668

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12777365

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15272270

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15236834


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