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A Review on Parkinson's Disease

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Abstract: *Parkinson's disease (PD) is a progressive neurodegenerative disorder that primarily affects movement control due to the loss of dopaminergic neurons in the substantia nigra region of the brain. It is characterized by tremors, muscle rigidity, bradykinesia (slowness of movement), and postural instability. Although the exact cause remains unclear, genetic factors, environmental toxins, and oxidative stress are known to contribute to its onset. Currently, there is no cure for Parkinson's disease, but various pharmacological treatments, including levodopa, dopamine agonists, and MAO-B inhibitors, aim to manage symptoms and improve quality of life. Non-pharmacological therapies such as physiotherapy, deep brain stimulation (DBS), and lifestyle modifications also play a significant role in disease management. Ongoing research is exploring new therapeutic strategies, including neuroprotective agents, gene therapy, and stem cell transplantation. This paper provides a comprehensive overview of the pathophysiology, clinical features, diagnostic approaches, and recent advances in the treatment of Parkinson's disease, highlighting the importance of multidisciplinary care in managing this complex condition.*

Keywords: Parkinson's disease, neurodegeneration, dopamine, substantia nigra, levodopa, deep brain stimulation, motor symptoms, neuroprotection, gene therapy

I. INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease, affecting millions of individuals worldwide, particularly the elderly population. First described by Dr. James Parkinson in 1817 as the "shaking palsy," the condition is characterized by a progressive decline in motor function due to the degeneration of dopaminergic neurons in the substantia nigra of the midbrain. The resulting dopamine deficiency disrupts normal movement regulation, leading to hallmark symptoms such as resting tremors, bradykinesia, muscular rigidity, and postural instability.

In addition to motor symptoms, Parkinson's disease also presents a wide range of non-motor manifestations, including depression, cognitive decline, sleep disturbances, and autonomic dysfunction, which significantly affect the patient's quality of life. While the exact etiology remains unknown, genetic mutations, oxidative stress, mitochondrial dysfunction, and environmental toxins have all been implicated in its pathogenesis.[1]

Currently, there is no definitive cure for Parkinson's disease. However, several symptom-relieving therapies, both pharmacological (such as levodopa) and surgical (like deep brain stimulation), have shown to improve patient outcomes. With increasing global life expectancy, the prevalence of Parkinson's disease is expected to rise, emphasizing the urgent need for enhanced diagnostic tools, early intervention strategies, and neuroprotective treatments.

This paper aims to explore the underlying mechanisms, clinical features, diagnostic criteria, and therapeutic advancements associated with Parkinson's disease to provide a deeper understanding of this debilitating neurological disorder.

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder that predominantly affects the motor system, but also presents a wide array of non-motor symptoms. It is the second most prevalent neurodegenerative disease globally, affecting approximately 1–2% of individuals over the age of 65. First documented by Dr. James Parkinson in 1817 as the "shaking palsy," PD has since become a major public health concern due to the increasing aging population.

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The primary pathological hallmark of PD is the loss of dopaminergic neurons in the substantia nigra pars compacta of the midbrain, leading to a substantial reduction of dopamine levels in the striatum. Dopamine is a critical neurotransmitter involved in regulating voluntary movement, mood, and certain cognitive functions. The progressive dopamine depletion results in the classical motor symptoms:[2]

- Resting tremor (shaking in hands, arms, or legs when muscles are relaxed)
- Bradykinesia (slowness of movement)
- Muscular rigidity (stiffness of limbs and trunk)
- Postural instability (impaired balance and coordination)

Beyond these, non-motor symptoms—including depression, anxiety, fatigue, constipation, olfactory dysfunction, sleep disturbances, and cognitive decline—can precede motor manifestations by years, making early diagnosis challenging.

The etiology of Parkinson's disease is multifactorial:[3]

1. Genetic factors – Mutations in genes such as SNCA, LRRK2, PARK7, PINK1, and GBA have been linked to familial PD cases.
2. Environmental factors – Exposure to pesticides, herbicides, and heavy metals; rural living; and well water consumption are associated with increased risk.
3. Cellular dysfunctions – Mitochondrial impairment, oxidative stress, protein misfolding (αsynuclein aggregation), and neuroinflammation contribute to neuronal death.

Treatment:

1. Medications (Mainstay of Parkinson's Treatment)

A. Levodopa/Carbidopa (Sinemet)

- Levodopa is the most effective drug for Parkinson's. It converts into dopamine in the brain, replacing what the brain no longer produces.
- Carbidopa prevents levodopa from breaking down before it reaches the brain, reducing side effects like nausea.
- Benefits: Major improvements in movement, especially in early stages.
- Side Effects: Long-term use can cause motor fluctuations (like "on-off" effects) and dyskinesias (involuntary movements).[4]

B. Dopamine Agonists (e.g., Pramipexole, Ropinirole, Rotigotine)

- Mimic dopamine in the brain and stimulate dopamine receptors.
- Less effective than levodopa for symptom relief, but longer-lasting.
- Often used in early stages or in combination with levodopa later.
- Benefits: Delay the need for levodopa.
- Side Effects: Sleepiness, hallucinations, compulsive behaviors (e.g., gambling, shopping), nausea.

C. MAO-B Inhibitors (e.g., Selegiline, Rasagiline, Safinamide)

- Block the enzyme monoamine oxidase B, which breaks down dopamine.
- Help increase dopamine levels in the brain.
- Can be used alone or with levodopa to enhance effect.
- Side Effects: Headache, insomnia, possible interaction with antidepressants.

D. COMT Inhibitors (e.g., Entacapone, Opicapone)

- Inhibit catechol-O-methyltransferase, an enzyme that breaks down levodopa.
- Taken alongside levodopa to extend its effectiveness.
- Side Effects: Diarrhea, orange urine, increased dyskinesia.

E. Amantadine

- Originally an antiviral, it helps reduce dyskinesias and has mild dopaminergic effects.
- Sometimes used early for tremor or later for involuntary movements.

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• Side Effects: Confusion, hallucinations, swelling in ankles, purple skin blotching (livedo reticularis).

F. Anticholinergics (e.g., Benztropine, Trihexyphenidyl)
• Reduce tremors by blocking acetylcholine (an opposing neurotransmitter).
• Mostly used in younger patients with tremor-predominant PD.
• Side Effects: Memory problems, dry mouth, constipation, confusion—so often avoided in older adults.

2. Surgical Options
A. Deep Brain Stimulation (DBS)
• A neurosurgical procedure where electrodes are implanted into specific brain areas (e.g., subthalamic nucleus or globus pallidus interna).
• Connected to a pacemaker-like device in the chest that sends electrical impulses to control motor symptoms.

Used For:
• Patients with motor fluctuations or dyskinesias not controlled well by medication.

Benefits:
• Reduces tremor, stiffness, and "off" time.
• May allow reduction of medication doses.

Risks:
• Surgical complications (bleeding, infection), changes in mood or cognition, hardware issues.

3. Physical and Supportive Therapies
A. Physical Therapy
• Improves mobility, balance, flexibility, and strength.
• Helps reduce risk of falls.

B. Occupational Therapy
• Teaches techniques and tools to manage daily activities (dressing, eating, bathing).
• Improves independence.

C. Speech and Language Therapy
• Addresses speech difficulties (soft voice, slurred speech) and swallowing problems.
• May include LSVT LOUD (a therapy to improve vocal strength).

4. Lifestyle and Support Strategies
A. Regular Exercise
• Shown to slow progression of symptoms and improve mood, mobility, and cognition.
• Examples: Walking, swimming, dancing, tai chi, yoga, strength training.

B. Nutrition
• No specific diet cures PD, but a balanced diet supports brain health.
• High-fiber foods and plenty of fluids help with constipation.
• Protein can interfere with levodopa absorption—some people benefit from protein redistribution (eating protein-rich foods later in the day).

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C. Mental Health Support

• Depression and anxiety are common—may require counseling or medication.
• Support groups and education can help individuals and caregivers cope.

5. Emerging and Advanced Therapies

A. Gene Therapy (Experimental)

• Aims to correct faulty genes or introduce new genes to help dopamine production.
• Still under clinical trials.

B. Stem Cell Therapy

• Investigating how to replace damaged neurons with healthy cells.
• Not yet approved for general use.[5]

C. New Drugs

• Research is ongoing into neuroprotective drugs that could slow or halt disease progression, not just manage symptoms.

Current treatment strategies focus on symptom management rather than disease modification. Pharmacological therapies such as levodopa-carbidopa, dopamine agonists, and MAO-B inhibitors remain the mainstay of motor symptom control. For advanced cases, deep brain stimulation (DBS) offers significant improvement in motor function.

With no known cure, ongoing research is exploring neuroprotective approaches, gene therapy, stem cell transplantation, and disease-modifying agents. Given the projected increase in PD prevalence due to global aging trends, there is an urgent need to improve early diagnosis, personalize therapy, and develop interventions that can slow or halt disease progression.[6]

This review aims to provide an in-depth analysis of the pathophysiology, clinical presentation, diagnostic challenges, and emerging treatment options for Parkinson's disease, thereby contributing to better patient care and future research directions.

Causes and Risk Factors of Parkinson's Disease

The exact cause of Parkinson's disease (PD) remains unknown, but research suggests that it arises from a complex interplay between genetic predisposition, environmental exposures, and agerelated changes. These factors lead to the progressive degeneration of dopaminergic neurons in the substantia nigra and abnormal accumulation of α-synuclein protein within Lewy bodies.

1. Genetic Factors

• Although most cases are sporadic, about 10–15% of PD patients have a family history of the disease.
• Key gene mutations linked to PD include:
o SNCA (α-synuclein) – Causes abnormal protein aggregation and Lewy body formation.
o LRRK2 (Leucine-rich repeat kinase 2) – The most common genetic cause of lateonset PD.[7]
o PINK1 & PARK7 (DJ-1) – Involved in mitochondrial function and oxidative stress defense.[8]
o GBA (Glucocerebrosidase) – Associated with lysosomal dysfunction and increased PD risk.
• Genetic PD often manifests at an earlier age than idiopathic PD.

2. Environmental Factors

Long-term exposure to certain environmental agents increases PD risk:
• Pesticides & Herbicides – Such as paraquat and rotenone, which impair mitochondrial function.
• Heavy Metals – Manganese, lead, and mercury exposure can cause neurotoxicity.
• Rural Living & Well Water Consumption – Linked to higher pesticide exposure.
• Industrial Solvents – Trichloroethylene and other organic solvents are associated with neuronal damage.

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3. Aging

• Advancing age is the strongest known risk factor for PD.

• The natural decline in dopaminergic neurons with age, combined with decreased antioxidant defenses, makes older individuals more vulnerable to neurodegeneration.

4. Oxidative Stress and Mitochondrial Dysfunction

• Dopaminergic neurons are particularly susceptible to oxidative damage due to dopamine metabolism.

• Impaired mitochondrial complex I activity leads to energy deficits and increased production of reactive oxygen species (ROS), triggering cell death.[9]

5. Neuroinflammation

• Chronic activation of microglia in the brain results in excessive release of inflammatory cytokines and neurotoxic substances, further contributing to neuronal damage.

6. Lifestyle and Other Risk Modifiers

• Traumatic Brain Injury (TBI) – Associated with increased PD risk.

• Low Physical Activity – Sedentary lifestyle may predispose to neurodegeneration.

• Dietary Factors – Low intake of antioxidants may increase vulnerability.[8]

• Protective Factors (observed in some studies) – Caffeine consumption, regular exercise, and smoking (nicotine) appear to reduce PD risk, although these are not recommended as prevention methods.

Pathophysiology of Parkinson's Disease

Parkinson's disease (PD) is primarily a progressive neurodegenerative disorder involving the loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and the presence of Lewy bodies, leading to disruption of motor control and other neurological functions.[10]

1. Degeneration of Dopaminergic Neurons

• The hallmark of PD is the gradual loss of neurons in the substantia nigra that produce
dopamine, a neurotransmitter essential for motor control.

• This degeneration leads to a dopamine deficit in the striatum (caudate nucleus and putamen), disturbing the basal ganglia-thalamocortical circuitry that regulates voluntary movement.

2. Role of Lewy Bodies and α-Synuclein Aggregation

• Lewy bodies are abnormal intracellular inclusions composed mainly of misfolded α-synuclein protein.

• In PD, α-synuclein undergoes pathological aggregation, disrupting cellular processes like protein degradation, synaptic function, and mitochondrial activity.

• These inclusions spread in a predictable pattern, starting in the brainstem and progressing to cortical areas (Braak staging).

3. Dopamine Deficiency and Motor Symptoms

• Normally, dopamine facilitates communication between the substantia nigra and the striatum, enabling smooth and coordinated muscle movements.

• Dopamine loss causes an imbalance between the direct (excitatory) and indirect (inhibitory)
pathways of the basal ganglia:

o Direct pathway → Facilitates movement (reduced in PD).

o Indirect pathway → Inhibits movement (overactive in PD).

• This imbalance manifests as bradykinesia, rigidity, tremors, and postural instability.

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4. Mitochondrial Dysfunction and Oxidative Stress[11]

• PD neurons show impaired mitochondrial complex I activity, leading to reduced ATP production and increased reactive oxygen species (ROS) generation.

• ROS cause oxidative damage to DNA, proteins, and lipids, triggering neuronal apoptosis.

5. Neuroinflammation

• Chronic activation of microglial cells in the substantia nigra releases pro-inflammatory cytokines (TNF-α, IL-1β) and reactive nitrogen species.

• This inflammatory environment accelerates neurodegeneration.

6. Non-Motor Pathophysiology

• Non-motor symptoms such as depression, sleep disturbances, and autonomic dysfunction occur due to degeneration in serotonergic, noradrenergic, and cholinergic systems.

• The locus coeruleus, dorsal motor nucleus of the vagus, and olfactory bulb are affected in early stages.

7. Braak's Hypothesis of PD Progression

• Suggests that PD pathology begins in the enteric nervous system and olfactory bulb, possibly due to environmental toxins or pathogens, and then spreads to the brain via the vagus nerve.

• This explains early non-motor symptoms like constipation and loss of smell before motor symptoms appear.[12]

Biomarkers

The National Institutes of Health and the U.S. Food and Drug Administration state that "a biomarker is not intended to measure how an individual feels, functions, or survives.[13]

Rather, it is a characterised trait that acts as a marker of pathogenic processes, normal biological processes, or biological reactions to exposures or interventions, including therapeutic ones. Biomarkers have been categorised into different groups by different researchers. While Surguchov identified clinical, imaging, pathological, biochemical, and genetic markers as possible PD biomarkers, some studies [14] have concentrated on clinical, biochemical, and neuroimaging biomarkers.Considering notable developments in fields like genetics, proteomics, neuroimaging, gut microbiome (GM),[15]and exosomal analysis[16], research on PD biomarkers is developing quickly. More accuracy in monitoring the course of Parkinson's disease and locating new targets for early intervention is possible when AI techniques are combined with biomarkers. The research that combines different biomarkers with AIbased methods is examined in the section that follows.

Table 1. Parkinson's disease biomarkers and their description

Type of biomarker	Description
Clinical	Clinical signs and symptoms that help with diagnosis and illness progression tracking are associated with these biomarkers. Cognitive decline, sleep difficulties, exhaustion, excessive perspiration, depression, idiopathic rapid eye movement sleep behaviour disorder, and constipation are examples of non-motor symptoms.[17] Tremors, stiffness, akinesia, and postural instability are examples of motor symptoms, along with two motor subgroups, including axial symptoms, gait abnormalities, and postural instability. The nigrostriatal system's dopamine-producing neurones' degeneration is most strongly correlated with bradykinesia and stiffness.[18]
Neuroimaging	These biomarkers identify structural and functional alterations in the brain, especially in areas like the substantia nigra and dopamine transporter systems, using imaging methods like MRI, SPECT, and PET.[19,20]
Biochemical & proteomic	Proteins, metabolites, and cellular alterations are only a few of the many chemicals and activities that are included in biochemical biomarkers. [21,22]Proteins implicated in the

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	illness process are the special focus of proteomic biomarkers. Saliva, blood, and cerebrospinal fluid all contain these indicators. Among the most researched are neuroinflammatory indicators, dopamine metabolites (HVA, DOPAC), and α-syn.[14,23,24]
Genetic	Most familial and sporadic forms of Parkinson's disease have been connected with genetic biomarkers. Gene mutations, including those in PRKN, LRRK2, and GBA, are known to be important genetic causes of the illness.[14,25]

Clinical Features of Parkinson's Disease

Parkinson's disease (PD) presents with a combination of motor and non-motor symptoms, which progress gradually over years. Early stages often involve subtle, unilateral symptoms, while advanced stages lead to significant functional impairment.

1. Motor Symptoms (Cardinal Features)

These result primarily from dopamine deficiency in the nigrostriatal pathway.

1. Tremor at Rest

o Typically "pill-rolling" tremor involving the thumb and forefinger.
o Most noticeable at rest and decreases with voluntary movement.
o Often starts unilaterally in the hand before spreading.

2. Bradykinesia

o Slowness of voluntary movement, difficulty initiating motion.
o Causes reduced arm swing, slow walking, and trouble with fine motor tasks (e.g., buttoning clothes).
o Leads to masked facies (reduced facial expression).

3. Muscle Rigidity

o Increased muscle tone with resistance to passive movement.
o Cogwheel rigidity (jerky resistance) or lead-pipe rigidity (smooth, constant resistance).
o Can involve neck, trunk, and limbs.[9]

4. Postural Instability

o Impaired balance and coordination.
o Difficulty maintaining upright posture, leading to frequent falls.
o Often develops in later stages.

2. Other Motor Manifestations

• Shuffling gait with small steps and stooped posture.
• Freezing of gait (temporary inability to move the feet).
• Micrographia (small, cramped handwriting).
• Hypophonia (soft speech) and monotone voice.

3. Non-Motor Symptoms

Non-motor features can appear years before motor symptoms, reflecting widespread neurodegeneration.[26]

1. Neuropsychiatric

o Depression, anxiety, apathy.
o Cognitive decline and Parkinson's disease dementia in later stages.
o Hallucinations (often medication-induced).

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2. Autonomic Dysfunction
o Constipation, urinary urgency/frequency.
o Orthostatic hypotension (drop in blood pressure upon standing).
o Sexual dysfunction, excessive sweating.

3. Sleep Disorders
o REM sleep behavior disorder (acting out dreams).
o Insomnia, excessive daytime sleepiness.

4. Sensory Symptoms
o Hyposmia or anosmia (reduced/loss of smell).
o Pain, paresthesia.

4. Disease Progression
• Symptoms often start asymmetrically and become bilateral with disease advancement.
• Hoehn and Yahr staging is commonly used to grade severity, from Stage 1 (mild, unilateral) to Stage 5 (wheelchair-bound/bedridden).

Diagnosis and Investigations of Parkinson's Disease[27]
Parkinson's disease (PD) is primarily a clinical diagnosis based on characteristic motor symptoms and response to dopaminergic therapy. There are no definitive laboratory tests, but imaging and specialized investigations help rule out other causes of parkinsonism.

1. Clinical Diagnosis
Diagnosis is guided by the UK Parkinson's Disease Society Brain Bank Criteria and MDS Clinical Diagnostic Criteria.

A. Core Features
• Bradykinesia (mandatory for diagnosis)
Plus at least one of the following:
o Muscular rigidity
o Rest tremor (4–6 Hz)
o Postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction

B. Supportive Features
• Asymmetry of motor symptoms
• Clear and dramatic response to dopaminergic medication
• Presence of levodopa-induced dyskinesia
• Rest tremor[28]

C. Red Flags / Exclusion Criteria
• Rapid progression
• Early autonomic failure
• Poor levodopa response
• Cerebellar or pyramidal signs
• Supranuclear gaze palsy
• History of repeated strokes or head injury

2. Investigations
A. Routine Laboratory Tests (mainly to exclude secondary causes)
• Complete blood count (CBC) – to rule out infection or systemic illness

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• Thyroid function tests – exclude hyperthyroidism or hypothyroidism causing tremor
• Vitamin B12 and folate levels – deficiency may cause neuropathy or cognitive symptoms
• Liver and renal function tests – exclude metabolic causes

B. Neuroimaging
• MRI Brain
o Usually normal in idiopathic PD o Used to exclude structural lesions (stroke, tumor, hydrocephalus) causing parkinsonism o Can show subtle changes in advanced disease
o CT ScanFor patients with contraindications to MRI or to rule out hemorrhage/mass[12]

C. Functional Imaging
• DaTSCAN (123I-FP-CIT SPECT)
o Assesses presynaptic dopaminergic function o Reduced uptake in striatum supports PD diagnosis o Helps differentiate PD from essential tremor and drug-induced parkinsonism
• PET Scan
o 18F-DOPA PET can visualize dopamine metabolism; more for research and select cases

D. Specialized Tests
• Olfactory testing – detects early hyposmia, common in prodromal PD
• Neuropsychological assessment – for cognitive and mood evaluation
• Autonomic function tests – assess orthostatic hypotension, heart rate variability[29]

3. Diagnostic Approach Summary
1. History & Physical Examination – focusing on motor and non-motor symptoms
2. Rule out secondary causes – via labs and imaging
3. Confirm dopamine deficiency – clinical + DaTSCAN if needed

4. Trial of dopaminergic therapy – significant improvement supports diagnosis
Complications and Prognosis of Parkinson's Disease
1. Complications
Parkinson's disease (PD) complications may arise from disease progression, treatment side effects, or both. They can be broadly divided into motor and non-motor categories.

A. Motor Complications
1. Motor Fluctuations
o Wearing-off: Return of symptoms before next medication dose.
o On–off phenomena: Sudden unpredictable changes in mobility.

2. Levodopa-Induced Dyskinesias
o Involuntary, erratic, writhing movements affecting limbs, trunk, or face.
o More common with long-term levodopa therapy, especially in younger patients.

3. Freezing of Gait
o Brief inability to step forward, leading to falls and injury risk.[1]

B. Non-Motor Complications
1. Cognitive Decline and Dementia
o Progressive impairment in memory, attention, and executive function.

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2. Neuropsychiatric Symptoms
o Depression, anxiety, hallucinations, psychosis (often medication-related).
3. Autonomic Dysfunction
o Orthostatic hypotension, urinary urgency/incontinence, constipation, sexual dysfunction.
4. Sleep Disorders
o REM sleep behavior disorder, insomnia, excessive daytime sleepiness.
5. Speech and Swallowing Difficulties
o Dysarthria, hypophonia, and dysphagia increase risk of aspiration pneumonia.[30]

C. General Complications
• Falls and Fractures due to postural instability.
• Aspiration Pneumonia from swallowing difficulties.
• Malnutrition due to eating problems and increased caloric needs from tremors.

2. Prognosis
• Disease Course: PD is progressive and irreversible, with the rate of progression varying between individuals.
• Life Expectancy: Slightly reduced compared to the general population; main causes of mortality are complications such as aspiration pneumonia, falls, and cardiovascular disease.
• Motor Symptoms: Typically respond well to medication initially, but responsiveness diminishes over time with increased treatment-related complications.
• Non-Motor Symptoms: Often become more disabling than motor symptoms in advanced stages.

Prognostic Factors
• Better Prognosis:
o Younger age at onset
o Good initial response to levodopa
o Tremor-dominant type

• Poor Prognosis:
o Early postural instability[31]
o Prominent non-motor symptoms at onset
o Early cognitive impairment

Long-Term Outlook
While PD cannot be cured, modern pharmacological, surgical, and rehabilitative therapies can significantly improve quality of life for many years. Early multidisciplinary intervention delays disability, but advanced disease often leads to substantial dependency in daily living.

Risk Factors for Parkinson's Disease[32]
Parkinson's disease (PD) is multifactorial in origin, with risk influenced by genetic, environmental, and lifestyle factors. While the exact cause remains unknown, several risk factors have been identified:
1. Non-Modifiable Risk Factors
1. Age
o The strongest known risk factor.
o PD incidence increases sharply after age 60; rare before 40 years.

2. Sex
o Men have a higher risk than women, possibly due to hormonal protection from estrogen in females.

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3. Genetic Predisposition

o Certain mutations (e.g., in SNCA, LRRK2, PARK2 genes) increase susceptibility.

o Family history of PD raises lifetime risk 2–3 times.

4. Ethnicity

o Some studies show slightly higher prevalence in Caucasians compared to Asians and Africans.

2. Modifiable / Environmental Risk Factors

1. Pesticide and Herbicide Exposure o Chronic exposure (e.g., paraquat, rotenone) is associated with increased PD risk.
2. Heavy Metal Exposure o Manganese, lead, and other metals may contribute to neurodegeneration.
3. Rural Living & Well Water Consumption o Often correlated with pesticide exposure.
4. Head Trauma

o History of repeated concussions (e.g., in boxing, football) increases risk.

5. Occupational Risks o Farming, welding, and industrial work involving solvents or metals.[28]

3. Possible Protective Factors (Inverse Association)

While not confirmed as causative, these factors have been associated with lower PD risk:

• Caffeine Consumption – Linked to reduced risk in several epidemiological studies.

• Smoking – Nicotine appears to have a neuroprotective effect, though smoking is not recommended due to other health risks.

• Physical Activity – Regular exercise may lower PD risk.[32]

II. CONCLUSION

Parkinson's disease is a progressive neurodegenerative disorder characterized primarily by motor symptoms such as tremors, rigidity, and bradykinesia, along with a range of non-motor manifestations that significantly affect quality of life. Although its exact cause remains unclear, a combination of genetic susceptibility, environmental exposures, and aging contribute to disease onset. Advances in neuroimaging, biomarker research, and molecular genetics have improved diagnostic accuracy, but there is still no definitive cure. Current treatment focuses on symptomatic relief through pharmacological agents like levodopa, dopamine agonists, and adjunct therapies, as well as surgical options such as deep brain stimulation. Comprehensive management also involves physiotherapy, occupational therapy, and psychological support to address both physical and emotional challenges. Ongoing research into disease-modifying treatments and neuroprotective strategies offers hope for slowing progression and improving patient outcomes in the future.

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