# Parkinson Disease and Other Movement Disorders

## Hypokinetic Disorders

### I Parkinson's Disease

1. Parkinson's Disease
2. Synchronized Neural Oscillations in PD
3. Autonomic Manifestations in PD
4. Neuropsychiatric Manifestations in PD
5. Sleep-Wake Disorders in PD
6. Diagnosis of PD
7. Conventional Treatment in PD
8. Conventional PD Treatment-Related Complications
9. Deep Brain Stimulation in PD
10. Continuous Dopaminergic Stimulation in PD
11. Pathology of PD
12. Genetic Parkinsonism

### II Parkinsonisms

1. Genetic Parkinsonism
2. Vascular Parkinsonism
3. Drug-Induced Parkinsonism
4. Multiple System Atrophy
5. Progressive Supranuclear Palsy
6. Corticobasal degeneration and Corticobasal Syndrome

---

**Editors**

Erik Wolters  
Christian Baumann  

International Association of Parkinsonism and Related Disorders  

Evidentia.med
Until the late twentieth century, Parkinson's disease (PD) was more or less considered a synonym to motor parkinsonism, the complex of mainly motor symptoms, originally described by James Parkinson and later on by Charcot as the clinical hallmark for Parkinson's disease (PD). In this disease, (motor) parkinsonism was considered the clinical expression of a dopaminergic denervation of the basal ganglia, as the result of an abortrophic degeneration of the dopamine-producing cells in the substantia nigra (SN). As of now, PD is considered rather the expression of a diffuse degeneration, affecting the peripheral and central nervous system. Indeed, PD, as of yet, is regarded a progressive α-synucleinopathic neurodegenerative disease, manifesting characteristically with both appendicular (hypokinesia, bradykinesia, rigidity and tremor) and/or axial (gait impairment, postural changes and postural instability) motor symptoms, though accompanied and in some cases even preceded by a multitude of non-motor signs and symptoms, with substantial variability among patients suffering this disease. Non-motor symptoms comprise autonomic dysfunctions such as cardiovascular, urogenital and gastro-intestinal manifestations, sleep-wake disorders, sensory disorders such as hyposmia or pain, impaired color vision, and neuropsychiatric disorders including mood disturbances, anxiety, cognitive deficits, dementia and psychosis. Symptomatic treatment in PD initially comprises oral dopaminomimetics, later on, to suppress dopaminomimetic-induced complications, continuous dopaminergic stimulation (CDS) with intrajejunal levodopa-carbidopa gel infusion, a subcutaneous apomorphin pump, or with deep brain stimulation (DBS) in order to continuously compensate for the intracerebral dopaminergic loss. Thanks to these therapeutical strategies, quality of life can be maintained into the latest stages of this disease. As of yet, protective treatment is not available although cell-based (1) and genetic therapies are promising.

Epidemiology

PD is a widespread disease with a world-wide incidence of about 10-20 in 100,000; a more recent overall annualized age- and gender-adjusted incidence reached 13.4 in 100,000 with a significant higher rate for men as for women, and with increasing rates in blacks (9.9), Asians (11.3), whites (13.6) and Hispanics (16.6), suggesting that the incidence varies by gender, race and ethnicity (2). PD cases are reported at all ages, but are uncommon in people aged under the age of 40 years. As the average age of onset in PD is established at about 60 years, it is principally considered to be a disease of the elderly. Younger patients, as a rule, are often found to suffer genetic parkinsonism.

Pathogenesis

Thanks to Braak and colleagues (3), following the identification of α-synuclein mutations and the realization that this protein was a core component of characteristic PD-related protein-
The same pathology is seen in incidental Lewy body disease (iLBD), which is considered an early, asymptomatic phase of PD and in dementia with Lewy bodies (DLB), hypothesized to be a special clinical manifestation of PD in which typical motor parkinsonism is preceded by cognitive deterioration. Although the aetiology in idiopathic PD is still essentially unknown, it is suggested that the synucleinopathy-driven neurodegeneration with Lewy bodies and neurites is the consequence of both cell-autonomous (originating within dying neurons) and non-cell-autonomous (originating from outside dying neurons) processes (5). Supposedly, cell autonomous processes comprise alterations in mitochondrial bioenergetics as well as a dysregulation of calcium homeostasis (with increased mitochondrial reactive oxygen species), both leading to mitochondrial damage and a defective autophagy (by lysosomal and ubiquitin proteasome systems), resulting in accumulation of intracellular α-synuclein oligomers and aggregates. In time, the burden of mitochondrial dysfunction will reach a pathological threshold, provoking neuronal dysfunction and ultimately cell death (5,6). Non-cell-autonomous processes, on top of this, are responsible for the contingent (supposedly prion-like) (7) spreading of the synuclein pathology over various (dopaminergic, cholinergic, serotonergic and noradrenergic) neuronal and non-neuronal (astrocytes, microglia, lymphocytes) cells across brain regions (5). As a matter of fact, the degeneration of some neurons in itself might also involve non-cell-autonomous mechanisms through their specific intra-neuronal connections (such as cholinergic or noradrenergic projections to dopaminergic neurons), or through a decrease of brain-derived neurotrophic factors (8,9). Risk factors contributing to synucleinopathic degeneration include autonomous activity, broad action potentials, low intrinsic calcium-buffering capacity, poorly myelinated axons and the use of monoamine transmit-