

Parkinsonism is a general term that refers to a group of neurological disorders with impairment of individuals' motor functions as a common clinical characteristic. These disorders have diverse pathological features and are also known under a group name of *Parkinsonian Syndromes or Disorders*. Bradykinesia, a slowness in initiation and carrying out of movements, is typically the earliest and most prominent and common motor symptom in *Parkinsonism*. Bradykinesia may be progressive, and over time, accompanied by other motor symptoms that include muscle rigidity with involvement of individual or entire muscle groups, tremor with involuntary shaking of muscles, and problems with keeping balance, all presenting in any combination, and with varying degree of intensity over time.

The diagnosis of *Parkinsonism* is made clinically. The diagnostic process involves evaluation of motor and non-motor symptomatology, neuropsychiatric and cognitive deficits as well as a detailed review of family and exposure history. Functional testing, including brain imaging techniques such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET), have been used increasingly to differentiate among different types of *Parkinsonisms*; however, their clinical validity is still under study.

Parkinsonisms are generally classified based on risk factors, clinical presentation with response/or lack thereof to known therapeutic agents, as well as disease pathology. The most recent 10th revision of the World Health Organization's International Statistical Classification of Diseases and Related Health Problems (*ICD-10 CM*) classifies most *Parkinsonisms* as Extraparamidal and Movement disorders, G20 through G26 (ICD-9 332.0).

Several risk factors for *Parkinsonism* have been identified to date. These include medications (neuroleptics, antipsychotic, metochlopramide); drugs (synthetic meperidine); infections (syphilis, post-encephalitis); metabolic (parathyroid, post-anoxic) and vascular (strokes, i.e., lower body parkinsonism) abnormalities as well as pathologic growth of, and/or injury to, brain structures, and are known under the group name of *Secondary Parkinsonisms*, classified altogether under ICD-10 G21.0 through G21.9 (ICD-9 332.1). Exposures to toxic agents such as carbon monoxide (CO), manganese (Mn) and carbon disulfide (CS₂) have also been known to present with *parkinsonian motor symptoms*, and are classified under toxic effects of each of the exposures respectively, i.e. carbon monoxide poisoning (ICD-10 T58.94 vs ICD-9 332.1); manganese, manganism (ICD-10 T57.2X1 vs ICD-9 332.1); and carbon disulfide (ICD-10 T65.4X1A vs ICD-9 982.2). These disorders may occur at any age, typically within days to weeks following the exposures; however, longer latency, up to a decade or more, especially with low, chronic exposures has not been ruled out in their pathogenesis.

Parkinson's disease (PD) is the most common disorder of all *Parkinsonisms*. It is estimated that 70-80% of all *Parkinsonism* cases are those of *PD*. This disease is often referred to as *Paralysis Agitans, Primary Parkinsonism, Hemiparkinsonism or Idiopathic Parkinsonism*. Up to 15% of *PD* cases may be hereditary, resulting from genetic mutations, with the remaining 85% potentially linked to a combination of genetic and external factors and exposures. Exposures to pesticides, solvents, polychlorinated biphenyls (PCBs) and metals have been shown in animal, human and experimental cell line model studies to be associated with increased incidence and risk of pathology consistent with Parkinson's Disease. Retrospective epidemiological studies have shown the increased risk of mortality from *PD* in PCB-exposed female workers, increased risk of

Parkinson's disease associated with exposures to trichloroethylene (TCE), a common industrial solvent, with metals, including copper and iron-copper alloys, and with pesticides, including insecticides and herbicides.

The clinical onset of motor function impairment in PD is typically over the age of 50 with risk increasing with age. It has been shown that the earliest motor symptoms of PD may be preceded, by up to 20 years and more, by the non-motor impairment in a person's sense of smell, and other non-specific symptoms including chronic constipation, depression, and sleep disorders. This pre-motor symptom stage is commonly referred to as the *prodromal stage of PD*, and efforts are currently underway to evaluate the effectiveness of clinical tests in the early diagnosis of this disease. The diagnostic gold standard of *PD* is still the post-mortem pathology, which in this disease, compared to other types of *Parkinsonism*, is preferential for degeneration of dopaminergic nerve cells in the substantia nigra part of the mid-brain, with abnormal protein depositions leading to impairment in the production of dopamine neurotransmitter.

Sets of diagnostic criteria have been adopted, based on the UK's Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria and more recently International Parkinson and Movement Disorder Society (MDS) Clinical/Research Diagnostic Criteria, to assist in the diagnosis of PD. Based on the primary diagnosis of the cardinal *Parkinsonian symptoms*, that is, bradykinesia, with at least one of the three other motor symptoms, supported by the evidence of response to dopamine substitution therapy, while excluding the secondary causes of *parkinsonism*, these criteria are used to differentiate between Parkinson's disease and other Parkinsonian disorders in the clinical diagnostic process and in research studies. Parkinson's disease is classified as an Extrapyrimal and Movement Disorder in the ICD 10 CM - G20 (ICD-9 332.0).

Parkinson-Plus syndromes are disorders that present with classical motor symptoms of *Parkinsonian syndrome* but eventually lack the response to dopamine substitute therapies. These disorders are characterized by diverse pathology, typically with more extensive and progressive neurodegeneration compared to PD. *Parkinson-Plus syndromes* are also known as *Atypical Parkinsonisms* and have been classified as Multiple Systems Atrophy (MSA) (ICD-10 G13.8 vs ICD 9 333.0), Progressive Supranuclear Palsy (PSP) (ICD-10 G23.9 vs ICD 9 333.0), Corticobasal Degeneration (CBD) (ICD -10 G31.85 vs ICD-9 331.6) and Lewy Body Dementia (LBD) (ICD -10 G31.83 vs ICD-9 331.82).

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