Chapter 8
Parkinson's Disease: Pathophysiology, Diagnosis, and Perspectives

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ABSTRACT

This chapter offers a comprehensive review of Parkinson's disease (PD), spanning from epidemiology to advanced treatment options. It delves into the neuropathology and the evolution of etiological theories, elucidating the genetic mechanisms and clinical subtypes of PD. The text outlines criteria for clinical diagnosis, including essential markers and exclusion factors, while introducing innovative diagnostic frameworks. The chapter is also an integrated guide discussing future research avenues for optimizing patient treatment and outcomes.

INTRODUCTION

First described by James Parkinson in 1817 in his seminal work, "An Essay on the Shaking Palsy," Parkinson's Disease (PD) stands as the most prevalent cause of parkinsonism (Obeso et al., 2017; Parkinson, 2002). PD is a chronic degenerative condition that is increasingly seen as a looming public health concern, especially in light of the aging demographics in emerging nations (Kalia & Lang, 2015; Tysnes & Storstein, 2017). This chapter aims to provide a comprehensive understanding of PD, encompassing its historical background, epidemiological scope, pathological

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mechanisms, etiological factors, genetic underpinnings, clinical manifestations, and diagnostic criteria.

Historical Background

Although partial accounts can be found in ancient Indian and Chinese texts, James Parkinson's 1817 monograph is considered the first full medical description of the disorder (Parkinson, 2002). The work succinctly delineates key features, as illustrated in the following translated excerpt: *"[...] Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellect being uninjured.*" Remarkably, only six cases were described in Parkinson's initial work, three of which were observed on the streets of London and one solely from a distance.

James Parkinson displayed remarkable accuracy and attention to detail. His observations covered a multitude of clinical facets that are still relevant today. Firstly, Parkinson's description of resting tremors, distinguishing them from those occurring during voluntary motion, was noteworthy. He recognized the unilateral onset of rest tremor, a key element in modern clinical diagnostic criteria. Parkinson also noted that rest tremors did not necessarily hinder fine motor acts, illustrating the complex nature of this symptom (Obeso et al., 2017). Moreover, he accurately documented gait abnormalities in PD, including shuffling, reduced step length, festination, and the forward-flexed posture now known as camptocormia.

However, Parkinson's essay did not explicitly mention rigidity or muscle stiffness, a cardinal feature of PD recognized later by Charcot (Li & Le, 2017). Additionally, he misinterpreted bradykinesia as weakness, failing to identify it as a distinct disease characteristic. Furthermore, Parkinson's essay offered insights into nonmotor symptoms, particularly in advanced disease stages, such as sleep disturbances, bowel issues, and urinary problems. While he couldn't examine these symptoms comprehensively due to limited patient interaction, his observations hinted at their presence. Lastly, Parkinson's account highlighted the slow and nearly imperceptible progression of the disease, emphasizing that patients often struggled to pinpoint its onset, a phenomenon still relevant in modern clinical practice.

Epidemiology

The epidemiological landscape of PD exhibits variability across different geographies and demographic subgroups (Tysnes & Storstein, 2017). Current data suggest that the global annual incidence of PD fluctuates between 4.5 and 16 cases per 100,000 population (Ascherio & Schwarzschild, 2016). This variance may be attributed to

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